COLLEGE OF AGRICULTURE AND APPLIED SCIENCE
LIBRARY
MAY 27 1952
MANHATTAN
KANSAS STATE

The New England
Journal of Medicine

Copyright, 1952, by the Massachusetts Medical Society

Volume 246 MAY 15, 1952 Number 20

THE VALUE OF CHOLANGIOGRAMS DURING BILIARY-TRACT SURGERY*

DONALD HIGHT, M.D.,† AND JAMES R. LINGLEY, M.D.‡

WORCESTER, MASSACHUSETTS

AN ACCURATE examination of the common duct should be a part of every operation on the extrahepatic biliary tract, except in the few cases in which the surgeon can be certain that the disease is limited to the gall bladder or in which the operative procedure must be minimal because of the poor condition of the patient. The history, physical findings and preoperative laboratory data may give valuable information concerning the patency of the ampulla or common duct, but frequently this information is neither complete nor infallible. The difficulty in detecting the presence of small stones in the common duct by palpation or in being certain after exploration of the duct that it contains no stones or other disease is recognized by all who perform this type of surgery.

Because of the need for an accurate and dependable method of examining the common duct, cholangiograms during the operative procedure were suggested by Cotte§ in 1929. It was hoped that they would be as reliable in disclosing disease of the biliary tract as pyelograms and studies with barium had proved to be in revealing abnormalities of the urinary and gastrointestinal tracts. However, the technical difficulties in obtaining satisfactory cholangiograms on the operating table at that time were considerable, and the films were frequently not satisfactory. Undoubtedly these deficiencies served as a deterrent to the general adoption of this procedure as a routine part of such operations. However, with modern equipment and methods, most of these difficulties have been overcome. With close co-operation among anesthetist, x-ray technician and surgeon, cholangiograms of good quality can now be obtained easily and almost routinely. Without such films, the radiologist cannot make his interpretation with a high degree of accuracy.

At first, operative cholangiograms were done at this hospital principally as a check after exploration and removal of stones from the common duct. The discovery by cholangiogram of stones that had been overlooked in several such cases soon demonstrated the value of this study. As experience with this procedure increased, its high percentage of accuracy became more generally appreciated by the members of the surgical staff at this hospital. Cholangiograms are now performed during the majority of operations on the extrahepatic biliary tract.

The purpose of this report is to describe the technic that has been employed in making operative cholangiograms at this hospital and to review our experience with them. By the adoption of a technic that eliminates most of the sources of error in interpretation and by the optimal timing of the cholangiogram during the operation so that little time is lost, the usual objections to this procedure can be overcome. We now consider the various indications for performing operative cholangiograms to be as follows: a history or laboratory data suggestive of partial or complete obstruction of the common duct, small stones or mud in the gall bladder, a dilated common duct and thickening along the common duct, particularly at the duodenum or head of the pancreas. Although we believe that a cholangiogram should always be made when any one of these conditions is present, the recent trend has been to perform them almost routinely to survey the common duct. This is done as one of the initial steps of the operation in all cases except those non-jaundice cases in which there are only large stones in the gall bladder and the cystic and common ducts are soft and not dilated and in non-jaundiced patients with acute cholecystitis or those who are poor risks and in whom only a minimal operative procedure such as cholecystostomy is planned.

Our routine technic for operations on the extrahepatic tract is as follows: The gall bladder is first freed from any overlying adhesions. The cystic duct and its junction with the common duct are next dissected out. The common duct is exposed sufficiently so that its size and the condition of the wall can be appraised. A cholangiogram is then

*Presented at the annual meeting of the New England Surgical Society, York Harbor, Maine, September 21, 1951.

†Assistant surgeon, Worcester Memorial Hospital.

‡Radiologist, Worcester Memorial and Worcester Hahenemann hospitals.

§Cotte, G., Sur l'exploration radiologique des voies biliaires avec injection de lipiodol apres cholecystostomie ou cholédocotomie. *Bull. et mém. Soc. nat de chir.* 55:863-871, 1929.

made, using a tonsil-type needle, which is inserted either directly into the common duct or through the cystic duct and on into the common duct. There are several advantages in using such a needle for inserting the radio-opaque medium and in making the cholangiogram at this time. Once the needle has been properly positioned in the common duct, it may be held in this position while preparations are made for taking the cholangiogram. Air bubbles,

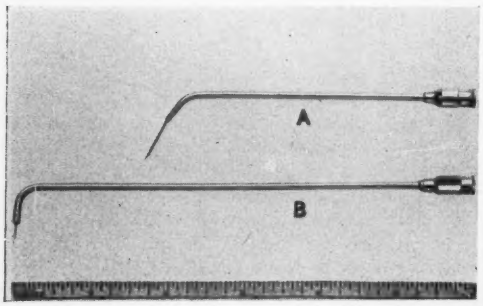

FIGURE 1. *Conventional Type of Needle Used for Tonsillectomy* (A) *and Needle Designed for Cholangiogram* (B).

which may be a source of error in reading cholangiograms, are easily eliminated from the needle. If the survey film shows a normal common duct and ampulla, the needle can be withdrawn and the cystic duct ligated with no leakage of bile. A needless exploration of the common duct can be avoided. In case the survey cholangiogram reveals disease of the duct or ampulla, this can be investigated and dealt with at once while the cystic duct and gall bladder are still intact. Then, if an obstruction is found that cannot be corrected, the gall bladder and cystic duct are still available if needed for a short-circuiting operation.

Although a straight needle may be used for the cholangiogram, it is difficult to keep this in proper position. To eliminate the danger of having the needle penetrate the opposite wall of the common duct, thereby permitting extravasation of the opaque medium, we use a needle that is similar to that used for infiltrating local anesthesia for tonsil operations. However, the needle that we use is 6 inches long, thereby permitting the attached syringe and the operator's hand to be well out of the operative field and the x-ray beam. The shank of the needle has a right-angle bend near the end into which a ¼" 23-gauge needle is fitted. This angulation permits the needle to be threaded into the cystic or common duct at about the same angle at which a needle is usually inserted in a vein. The short length of the 23-gauge needle extending beyond the shoulder of the main shaft ensures the easy maintenance of the proper position of the needle in the lumen of the common duct while all instruments and sponges are being withdrawn from the wound. After the proper position of the needle is again checked by the aspiration of bile, the entire field is covered with a sterile sheet. A grid-fronted cassette is then slid into a portable cassette tunnel that previously had been placed on the table in the proper position beneath the patient before the anesthesia was started. The mobile tube stand is wheeled to the table and the tube is moved into the proper position over the gall-bladder area. The technical factors for a 150-lb. patient are as follows: 150 Ma., 2/10 second, 30-inch distance, 80 K.V.P.

When the x-ray technician indicates that the equipment is ready, the surgeon injects 10 cc. of a

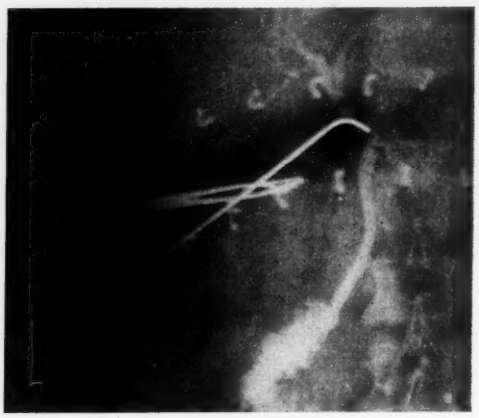

FIGURE 2. *Case 1: Normal Cholangiogram.*

40 per cent Diodrast solution. As the last cubic centimeter is being injected, he signals to the technician and the anesthetist so that the exposure can be made when there is no respiratory motion. Seven cc. of Diodrast solution diluted with 3 cc. of saline is usually used, since full-strength Diodrast is so dense that its shadow may obscure small stones in the common duct. Occasionally, Diodrast solution diluted even further is used when a thin shadow is desired.

Once the exposure has been made, the film is immediately processed. While this is being done the operation can be continued, to minimize the amount of time lost. The cystic artery is dissected out and a ligature is passed around it in preparation for ligation. If the cholangiogram is not yet ready to be viewed, serosal flaps can be raised along either side of the gall bladder. Usually the film is ready shortly after that dissection has been started, so it

is now viewed by the surgeon. If there is any question in his mind about the presence or absence of stones, the radiologist is called to the operating room in consultation.

If there are no stones or obstruction, the needle is removed and the cystic duct is ligated flush with the common duct. When evidence suggestive of stones or other disease is found, the common duct is opened and explored. Once the common duct has been opened for removal of stones or other disease, check cholangiograms are usually made using a "T" tube or catheter sutured in the duct.

The tube and duct are filled with saline solution to eliminate all air bubbles before the radio-opaque solution is injected. If shadows that are suspected as due to air bubbles are seen in the cholangiogram, a repeat film after another 10 cc. of solution has been injected will often give additional evidence that will aid in determining whether or not the shadow is due to a stone.

During the past two years 223 patients at this hospital underwent surgery on the extrahepatic biliary tract. In this group 115 had cholangiograms during the operative procedure. Although operative cholangiograms were done only occasionally at first, as our equipment and technic improved the accuracy and value of this procedure became more generally appreciated; hence during the last two months of this study, operative cholangiograms were done on 81.4 per cent of the cases submitted to biliary-tract surgery. Analysis shows that of the 115 operative cholangiograms made 96 or 83.4 per cent were considered satisfactory by the radiologist. Again, during the last two months of this study, of the 27 operative cholangiograms performed during that time all but one were considered satisfactory by the radiologist.

In this series, the operative cholangiograms were positive in 27, or 23.4 per cent of the cases. A diagnosis of stones was made in 22 cases, of stenosis of the ampulla in 4 cases and of tumor of the common duct in one case. In one additional case a congenital anomaly was discovered. This cholangiogram showed the ampulla of the common duct to be located in a diverticulum of the second portion of the duodenum. Stones were removed in 19 of the 22 cases in which the cholangiograms were interpreted

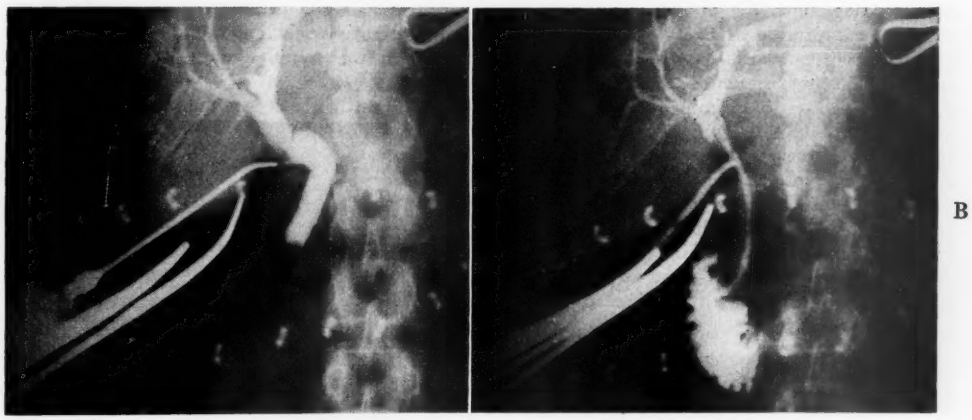

FIGURE 3. *Cholangiograms from Case 2.*
A = *Survey cholangiogram, revealing a dilated common duci and obstruction at the ampulla. B = Cholangiogram taken after a stone had been removed from the common duct, revealing a normal duct with prompt emptying into the duodenum.*

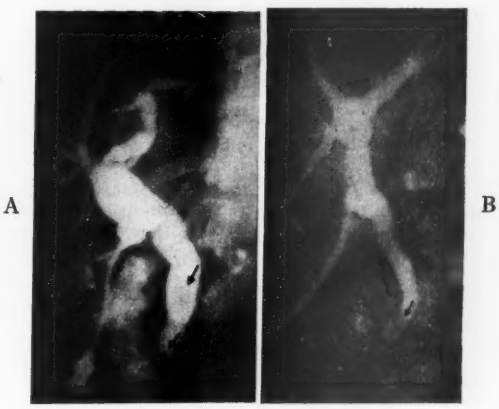

FIGURE 4. *Cholangiograms from Case 3.*
A = *cholangiogram showing calculi in the common duct.* B = *second cholangiogram, taken after exploration of the common duct, showing that a stone impacted in the ampulla had been missed.*

as showing stones. In 3 cases the cholangiograms were reported as showing evidence of a stone, but none were found. In one of these (Case 4), exploration by duodenotomy and direct inspection of the ampulla was negative. The shadow just within the ampulla was so characteristic of a stone in this case that when no stone was recovered after thorough exploration the possibility of the stone's having been pushed through into the duodenum prior to duodenotomy was considered likely. One of the other cases that was reported to have a positive operative cholangiogram but in which the exploration was negative was later re-examined by postoperative cholangiogram. This also revealed a shadow indicative of a stone, so the patient was re-explored and a stone was removed. During our early experience with cholangiograms, one of the survey films revealed a deformity of the common duct that was interpreted as being caused by the cannula through which the dye was injected, and it was read as negative. The patient later returned with evidence of common-

FIGURE 5. *Operative Cholangiogram from Case 4, Showing a Large Stone in the Ampulla.*

duct obstruction. At operation the obstruction was found to be caused by a tumor that had arisen in the common duct at the site of the previously noted deformity. With the standardization of technic and improved quality of films, errors such as this may be eliminated.

In reviewing the cases treated before operative cholangiograms were frequently used, there were 9 occasions in which the common duct was explored without a survey film or a post-exploration check-up film. In this group of 9 cases, exploration was negative in 5 cases and yielded stones in 3 cases. One tumor of the common duct was missed by exploration. This was later shown by cholangiogram. Needless to say, the 5 negative explorations might have been avoided had a survey cholangiogram been done.

In further assessing the value of operative cholangiograms, it is important to know how many stones or other diseases were missed by cholangiograms. In this entire series of 115 cases there were 3 such errors. In 1 a tumor of the common duct was overlooked; this case has already been reviewed. There were 2 cases in which operative cholangiograms taken after stones had been removed from the common duct were interpreted as negative, but check postoperative cholangiograms taken before the tube in the common duct was removed revealed

FIGURE 6. *Operative Cholangiogram from Case 5, Showing a Filling Defect in the Common Duct That Proved to be Due to Carcinoma.*

stones remaining in the common duct. These two patients were re-explored and the stones were removed.

It is interesting to note that in the group of 98 cases in which no operative cholangiogram was made disease of the common duct was missed in 3. One patient was later found to have a tumor of the common duct, and 2 patients were later re-operated on and stones removed from the common duct. If operative cholangiograms had been made in these cases, re-operation with the additional risk of surgery, discomfort and expense could have been avoided.

Since cholangiograms made during the postoperative period have revealed residual stones in a few cases despite exploration or inconclusive operative cholangiograms, we have adopted the practice of performing them routinely before the common-duct tube is removed in those cases in which it is doubted that all the stones in the common duct have been removed. We have had no known cases in

COLLEGE OF AGRICULTURE AND APPLIED SCIENCE LIBRARY MAR 27 1952 MANHATTAN, KANSAS

which stones have been missed by the postoperative cholangiograms.

Discussion

These figures indicate that without operative cholangiograms the common duct will be explored unnecessarily in many cases and that in others stones or other disease will be overlooked despite careful exploration. Operative cholangiograms of good quality will enable the radiologist to make accurate interpretations in most cases, so that such mistakes can be avoided. The importance of good films cannot be overemphasized, as slight motion or hazy film shadows will make interpretation difficult and more subject to error. High speed x-ray equipment and a grid-fronted cassette are essential for making satisfactory films.

Summary

A series of 115 cases in which operative cholangiograms were made during surgery on the extrahepatic biliary tract are reviewed.

The indications for and against operative cholangiograms and the value of routine survey films of the common duct are discussed.

The x-ray equipment and the details of the technic that is employed at this hospital in performing operative cholangiograms is described. With the aid of modern equipment and this technic, films of good quality can now be obtained almost routinely. With such films errors in interpretation can be minimized.

The radiologist considered 83.4 per cent of the films in this series of 115 cholangiograms to be satisfactory. The films were diagnosed as positive in 27 or 23.4 per cent of the cases, and a negative diagnosis was made in 78. Two errors in the latter group were discovered by postoperative cholangiograms that revealed residual stones.

Cholangiograms made during the postoperative period are a valuable check when there is any doubt that all stones have been removed from the common duct.

It is our opinion that although operative cholangiograms may not always be infallible they can be made quickly and can be of such quality that the radiologist can make a highly accurate interpretation. This information is of great value in avoiding needless exploration of the common duct. When stones are present, a fairly accurate method of examination is available to determine when all stones have been removed.

The reliability of this method of examination of the common duct is considered such at this hospital that cholangiograms are made almost routinely during operations on the extrahepatic biliary tract.

THE DOCTOR OF TOMORROW AND FEDERAL MEDICAL SERVICES*

Robert Collier Page, M.D.†

NEW YORK CITY

GENERAL MARSHALL, as Secretary of Defense, has stated that the Government is thinking in terms of a possible ten-year tension — a prolonged tension rather than a full-fledged war. What does this mean to the medical profession?

Thirteen thousand physicians will be continually needed for active military duty, which means that for every 11.5 doctors who are engaged in private practice 1 doctor will be in uniform. Other governmental agencies presently engage the full-time professional services of 6.776 doctors. As of December 1950, there was 1 physician out of every 15.75 in the United States in governmental service of one type or another; likewise 1.5 nurses for every 15.75 duly registered were on Government payrolls.

It has been suggested[1] that all graduates serve a prescribed period of time after completion of medical training on the assumption that such a plan has greater merit than to expand the regular military medical services or to interrupt the academic programs. What actual effect this state of affairs will ultimately have on the caliber of medical service available to the average American citizen remains to be seen. We as doctors are presently faced with a problem that vitally affects us both professionally and as United States citizens. The subtle expansion, — the vast and uncontrolled growth of federal medical systems in recent years, — has produced serious maldistribution and underutilization of medical manpower with increasingly adverse impact on all voluntary and community facilities.

You will agree, I am sure, with the statement that the present attitude of the average physician who had active military service in World War II toward Government medical service leaves much to be desired.

Adverse developments were clearly foreseen by the bipartisan Hoover Commission when it made its historic report to Congress in 1949. The Commission found that the Federal Government today is obligated, in whole or in part, for the care of some 24,000,000 citizens, of whom 19,000,000 are veterans, and also, under the Hill–Burton Act, for assistance to voluntary and community hospitals in building or expansion operations. Because the Government

*Presented before the tenth annual meeting of the New England Postgraduate Assembly, Boston, Massachusetts, November 7, 1951.

†Chairman, National Doctors Committee for Improved Federal Medical Service.

has no co-ordinated plan of operation for its facilities, the result has been waste, inefficiency and much confusion through the duplicating operations of 5 large and over 30 smaller Federal medical systems.

These agencies, which include the Army, Navy Air Corps, Veterans Administration and the Public Health Service, are operating completely independently of each other. Even among branches of the military service there is still insufficient co-ordination. Soldiers, for example, are not easily or efficiently admitted to Navy hospitals in the United States, and sailors have equal difficulty in obtaining admittance to Army hospitals. Sick or injured men in active military service are barred from Veterans Administration institutions. Facilities of one agency are often crowded while those of a different branch, quite possibly nearby, are half empty and their personnel correspondingly idle.[2]

Federal medical activities now cost above $2,000,000,000 a year.[3] The Hoover Commission, aided by a research "task force" of experienced physicians and hospital administrators, delved deeply into every detail of these activities in a study lasting more than a year. It is the Commission's recommendation that Federal medical facilities be unified. This would mean a "Department of Health," by which means, the Commission contends, it would be possible to effect economy in manpower, space and equipment. It would assure wise use of professional talent and proper economic usage of existing facilities.

The Hoover Commission[4] was unanimously created by Congress and consisted of 12 high-minded men, 6 Democrats and 6 Republicans, selected equally by President Truman and the presiding officers of the Senate and House of Representatives. At President Truman's suggestion, former President Herbert Hoover was named chairman. The commissioners were aided by 24 research committees called "task forces," comprising 300 eminent experts in their fields. Members of the Commission served for fourteen months or more without pay and sometimes to the neglect of their regular affairs. Each member had an earnest desire to serve his country.

Eleven of the 17 men who formed the *medical* task force were physicians; the rest were experts in hospital administration. Seven were veterans. It was on the data supplied by this task force that the Commision recommended unification of the Federal medical services. These recommendations are now before Congress, embodied in Senate Bill S.1140 and House Bill H.R. 3305.

As a member of the medical profession, each practicing physician has a personal interest and should play a role in any program that would provide a more equitable distribution of physicians and nurses, the greatest use of all medical facilities and more co-ordinated action in regard to hospital construction. From the viewpoint of efficiency and economy, to say nothing of preparedness for a possible major catastrophe, these subjects merit personal consideration by all members of our profession.

There is a wide divergence of opinion about this entire problem. It is extremely difficult to reconcile conflicting beliefs. The groups that favor, as well as those that oppose, suggested solutions of the problem are composed of large numbers of influential persons with many powerful supporters. For example, the Health Resources Advisory Committee of the Office of Defense Mobilization has estimated that there will be a shortage of 22,000 doctors and 49,200 nurses by 1954.[5]

It has been suggested that enrollment in the medical schools be increased 15 per cent.[6] On the other hand, it has been demonstrated that 40 per cent of the nation's physicians were in military service in World War II, leaving 60 per cent to care for the civilian population.[2] In this latter view, an enrollment increase would result in a surplus of doctors by 1960.[7]

Rappleye[8] of Columbia disputes the fact that any potential shortage can be remedied by a speed-up in medical education. Recently Dr. Rappleye pointed out that increased enrollment in medical schools would carry a threat to the quality of the doctors produced. The solution, he states, "lies in a better distribution of doctors."

Currently we hear that the training of competent doctors and medical scientists is imperiled by the financial crisis in the medical schools.[9] We hear also that if this condition is allowed to continue it will adversely affect the nation's health. Educators and economists[10] have remarked that there are potential dangers to academic freedom in the situation.

All this presents definite problems, and the question is: What is to be done about it? Again, there is a diversity of opinion.

General Simmons, dean of the Harvard School of Public Health, in a speech before the Philadelphia College of Physicians, recommended unification of all Government medical services, except those of the Armed Forces, in a "Department of Health" of Cabinet rank. This, he said, would permit "a closely integrated national program to conserve the health of both the civil population and the Armed Forces."

The American Medical Association,[11] in a statement submitted to the Senate Committee on Labor and Public Welfare on July 11, 1950, agreed in principle with the recommendations of the Hoover Commission but objected to some of the provisions of S.2008, which would effect unification of the medical services, and suggested further study by the Senate.

The American Legion[12] has announced itself in its publications and through the testimony of its former National Commander, George N. Craig, before the House Committee on Expenditures on

July 29, 1950, as opposed to any reorganization affecting Veterans Administration medical agencies.

Thus, there is a wide field for discussion of this problem in order that these differences may be ironed out.

The conditions of inefficiency and waste in the Government's medical services are astonishing, especially to physicians. But more astonishing still is the fact that very little if anything has been done about them.

For two years legislation intended to correct conditions in the 35 Government medical agencies has lain on the desks of members of Congress. This delay in acting on such bills is regrettable in these days of national emergency, when the needs of the Armed Services and the civilian population demand the most effective use of the nation's medical manpower and facilities.

In its report to the Hoover Commission, the medical task force stated:

> For the faults which we have found, we blame principally the competitive organization climate in which the various agencies have striven to maintain themselves, rather than the agencies themselves.
>
> This enormous and expanding enterprise is devoid of any central plan. Four large and various smaller agencies obtain funds and build hospitals, each to care for its own clientele. They compete with each other for scarce personnel. Generally, none of them considers the facilities of or the needs of the others. No one has responsibility for any overall plan. There is not even any clear definition of certain classes of beneficiaries for whom care is to be planned.
>
> The Government is moving into uncalculated obligations without an understanding of their ultimate cost, the lack of professional man-power available to discharge them or the adverse affect upon the hospital system of the country.
>
> In general, in federal medical services, the authority of the professional medical personnel is limited and actually subordinate to that of the non-medical personnel.
>
> In the Veterans Administration, lay control by the administrator includes decision, not only of what hospitals will be built, but also of the location. Both of these matters should be initiated and finally decided by the highest medical authority in the agency.
>
> The purchase of purely medical items, which we may describe loosely as those used to treat patients, is a technical function requiring extensive professional knowledge and continuing adaption to the changing techniques of the medical profession. This principle is violated in the veterans administration in which the supply service is on an equal basis with and wholly independent of the Department of Medicine and Surgery.[13]

The survey by the task force uncovered incredible examples of confusion and ineptitude in Government medical affairs. For example, 87 per cent of the cases in Veterans Administration hospitals have non-service-connected injuries or illnesses. Out of 577,715 cases admitted during the last twelve-month period, only 79,965 or 13 per cent were service connected.[14] According to the Hoover Commission, 4 Army and Air Force hospitals in the New York area alone might well be closed, with a consequent 80 per cent reduction in medical personnel. In the Los Angeles area, 5 hospitals, or about 30 per cent of the total capacity in 12 Federal hospitals, could be done away with, and in the San Diego area it was held that 2 or 3 hospitals could do the work of 10.

The Veterans Administration had an excess of voluminous printed instructions[15] on internal methods and procedures that defy intelligent execution. It published 88 different manuals, 665 varieties of technical bulletins and over 400 circulars of various kinds. The Veterans Administration expanded 9 pages of Public Law into 994 pages of "explanation." To cut this red tape, a thorough reorganization of the Veterans Administration was advocated. Although by now there may have been some change in the situation, the alarming thing is that such conditions have been permitted to exist at all.

The unification of the armed services has helped governmental medical services somewhat. It is paving the way for a more standardized and consequently more efficient and economical approach to the Government's already multitudinous commitments in the field of medicine. Under a recent directive of the Department of Defense, "any member of the Army, Navy or Air Force may be admitted to the nearest military hospital regardless of the service which operates it."[16] Acting under the authority of the Secretary of Defense, the Armed Forces Medical Policy Council in 1950 put into effect a unification of the medical services of the three branches of the Armed Forces in Korea. This policy has extended even to the Veterans Administration hospitals. In the period from February to June, 1951 (inclusive), 1512 casualties from the Korean Theater were transported to the United States and placed in Veterans Administration hospitals.

However, in response to statements that have appeared in the press[17] and medical publications[1, 18] extolling improvements of military medical services, Dr. A. R. Koontz[19] has contended that the Surgeon General is greatly handicapped under the present Army organization setup in his responsibility for the care of casualties in wartime. He stated:

> The Surgeon General has no real control over what goes on medically in any theater of war. Often theater commanders select their theater surgeons because they happen to like them personally and regardless of whether they have any qualifications for the job or not. Theater Commanders seldom know enough about the technical problems involved to be able to judge the professional qualifications of the Surgeon.

There is another aspect of the unregulated expansion of the Federal medical services without coordination. It is the effect it has upon the Federal operation under the Hill–Burton Act. This Act permits the Government to assume one third of the expense of constructing or enlarging voluntary community hospitals. It is intended to assure a nationwide system of such hospitals for the protection of the civilian population and to serve as auxiliary to government hospitals in times of great emergency. Up to the end of the 1951 fiscal year, June 30, the

Government approved construction of 1596 projects, of which 494 are completed and 990 are under construction. The total cost to the Government is $433,978,400.[20]

Because there is no over-all program of hospital construction, this plan has been interfered with by the construction of Federal hospitals in the neighborhood of voluntary hospitals that, because they offer higher pay and more security for personnel, have in some places seriously crippled the staffs of these community hospitals.

Table 1 illustrates the dangers resulting from a lack of co-ordination between the Veterans Administration and the military authorities. In some sections large Veterans Administration hospitals are being built while nearby military hospitals are being shut down. These are a few outstanding examples of many similar cases throughout the country.

TABLE 1. *Lack of Co-ordination — 1949.*[21]

PLANNED VETERANS ADMINISTRATION HOSPITALS		
Boston, Massachusetts	GMS	1000 beds
Brockton, Massachusetts	GMS	1000 beds
Philadelphia, Pennsylvania	GMS	500 beds
Atlanta, Georgia	GMS	500 beds
Ann Arbor, Michigan	GMS	500 beds
Los Angeles, California	N.P.	1000 beds
MILITARY HOSPITALS BEING CLOSED		
Murphy General Hospital, Waltham, Massachusetts		715 beds
Valley Forge General Hospital, Phoenixville, Pennsylvania		1650 beds
Oliver General Hospital, Augusta, Georgia		1500 beds
Percy Jones General Hospital, Battle Creek, Michigan		1200 beds
U. S. Naval Hospital, Long Beach, California		1500 beds

Not only is there duplication and lack of co-ordination in the urban areas, but extreme dislocation has been found where hospitals were built for political considerations. The Miles City, Montana, hospital is one of the many.

Miles City has a population of 9184 and, with a Public Health Service estimated need for hospitals at 3½ beds per 1000 persons, is already well serviced with a hospital general medical service of 135 beds. There are 13 physicians in Miles City, of whom 6 would be unable to aid the Veterans Administration hospital. The result is that the new Veterans Administration hospital has a layman manager, no medical director, no chief of medical services and no patients. Moreover, the location of Miles City (350 miles from the nearest railroad division point) makes it extremely inconvenient for it to be reached by Veterans Administration patients. At $50,000 a bed, this is an extraordinary waste.[22]

There are striking examples of lack of co-ordination in this area, as is shown in Figure 1. The Veterans Administration was planning a thousand-bed hospital in Boston when the Murphy General Hospital at Waltham with 715 beds was being disbanded. The Administration was planning a thousand-bed hospital in Brockton while the Government was closing down the Valley Forge General Hospital at Phoenixville, Pennsylvania, which accommodates 1650 patients.

Two more striking examples — a large new Veterans Administration hospital was recently opened in West Virginia with great fanfare. At last report, it had a staff of two physicians and no patients. In Dublin, Georgia, there stands a thousand-bed hospital in which the Veterans Administration is authorized to staff and use 500 beds. At this time only 300 beds can be used because of the staff problem and because transportation facilities to this installation were so poor that an airfield had to be built to bring the patients in. The nearest Pullman-sleeper facilities are 53 miles away at Macon, Georgia.[22]

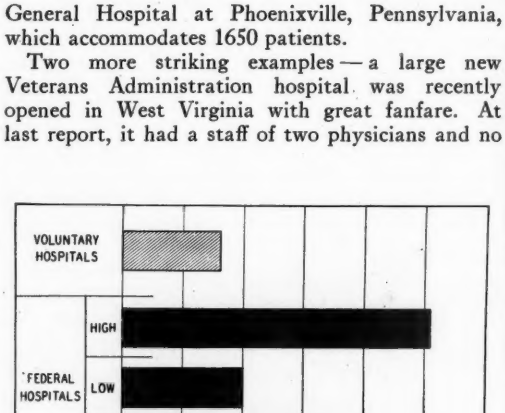

FIGURE 1. *Construction Costs (by Beds) of Federal and Voluntary Hospitals: 1949.*

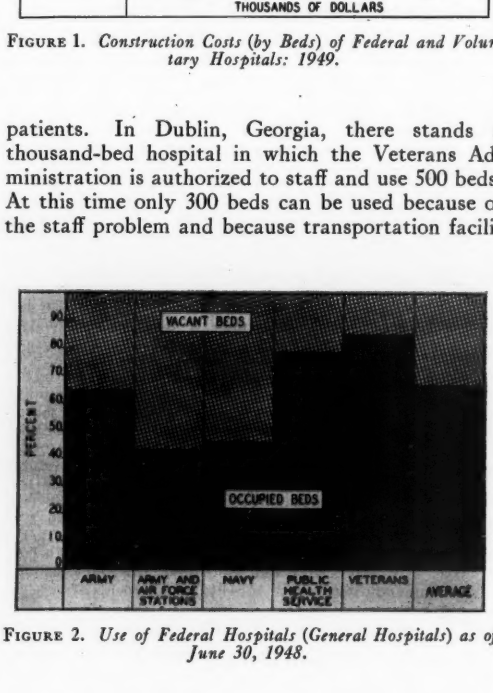

FIGURE 2. *Use of Federal Hospitals (General Hospitals) as of June 30, 1948.*

The Government is therefore doing an injury to the civilian population and to the medical profession by stockpiling physicians in unnecessary institutions.

Another disservice results from laxity in the enforcement of law by which many veterans obtain

admission to Government hospitals for free care simply by signing a "paupers' oath" that they are unable to pay. According to Senator Paul H. Douglas of Illinois, an outstanding exponent of economy in government, this practice costs the Government several hundred millions annually.[23]

There, in brief, is a picture of the present Federal medical system. All the evidence, — the findings of the medical experts who have studied the Federal medical system for the bipartisan Hoover Commission, the experience of hundreds of private physicians and many thousands of veterans who have been confined in Federal hospitals, — points strongly to two basic conclusions:

Government medical services, through the years, have grown without over-all supervision into a confused, extravagant collection of competing agencies. They are wasting medical manpower and facilities and getting in each other's way. Moreover, there is a maldistribution of doctors, to the detriment of large areas of the population.

Every action of the Government in the area of medicine affects the private practitioner in one way or another. Our Federal Government[24] is by far the largest single employer of doctors and the biggest operator of hospitals in the land.

These are the facts. Each physician must voice his objections to the Government for ignoring the needs of the civilian population by the wasteful use of medical manpower by building more hospitals than it can staff and allowing lay officials to oversee doctors in the purely medical functions of the Veterans Administration.

The present situation calls for action — action by doctors. In the opinions of many, the bills now before Congress for creation of a Federal Department of Health (S. 1140 and H.R. 3688 and 3305) are good bills. They would cure many of the evils that presently exist. Others, however, think that the bills are not strong enough, that the medical profession is not adequately protected. And still others, of course, believe that nothing should be done.

That something will be done, however, is clear. It is also extremely clear that unless the doctors of the country make their voices heard in Congress, some legislation engineered by layman groups may be passed that could have disastrous results for the medical profession. Certainly Congress cannot be blamed if they are not informed of how the doctors feel about this important legislation. Certainly Congress cannot be blamed if medical men have not enough self-interest to state their position.

I want to emphasize as strongly as possible that the nation's health is first of all a medical problem. Health maintenance is the business of the medical profession. Its ranks are increased each year by the graduation of 7000 students from 79 medical schools.[25]

The annual cost of medical education in the country is $80,136,000.[25] These young physicians plan a life of service to the public and they, with their elders, are properly disturbed by unregulated operations of the Government in the field of health and by the dislocation and maldistribution of doctors by Government agencies. Therefore, in the forthcoming hearings on the reorganization bills designed to streamline the confused setup of Government medical agencies, the views of the medical profession will be essential and should merit attention.

The huge $2,000,000,000 structure, involving the care of 24,000,000 citizens legally entitled to Federal health service, was created and expanded, even in its professional and medical aspects, by laymen.[26]

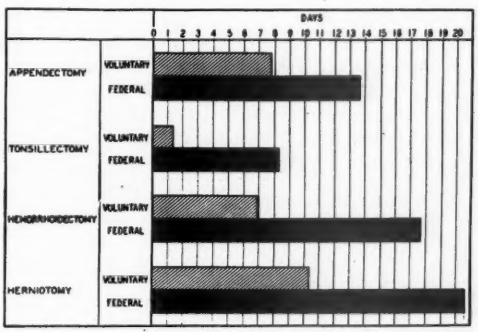

FIGURE 3. *Length of Stay in Federal and Voluntary Hospitals: 1949.*

Certain physicians like Dr. Paul Magnuson,[27] former medical director of the Veterans Administration, raised protests against lay authority over purely medical matters, without avail.

And now, unless we doctors follow through and see to it that the recommendations of the Hoover Report or some other remedial legislation is acted on to correct conditions in the Federal system, laymen will again take over and we could easily find ourselves back where we started.

I have told you what the Commission found — a vast, competitive organization of which the parts cared nothing about the whole and by which unnecessary hospitals were built in inaccessible places to please some politicians — and how, in empire-building competition, the various agencies competed for scarce medical personnel and enticed away, by offers of higher salaries, medical personnel from community hospitals sponsored by the Government under the Hill–Burton Act.[28] In stating these recommendations the Commission predicted that these results would follow their enactment:

> The general standard of Federal medical care would be improved.

There would be a central supervision of the major Federal medical care, public health and medical research activities. Unified responsibility is the key to good management. The President, the Congress, and the public could look to one man for results.

Construction costs could be standardized and reduced.

Federal hospitals could be utilized to the fullest extent by eliminating present distinctions concerning the particular types of beneficiaries for which each can care. A patient is a patient whether he is a veteran, a merchant seaman, or a member of the Army, Navy or Air Force.

The medical manpower at the call of the Federal Government could be used to the fullest extent, and present deficits in skilled personnel could be greatly reduced.

The need of any draft of medical manpower in time of peace would be greatly lessened.

The cost of health and medical services would be clearly identified and known to Congress.

The facilities of private hospitals and the skills of physicians in private life and in the universities could be utilized far more effectively than at present.[29]

The bills now before Congress contain the recommendations of physicians who had in mind the effects of the present system on the welfare of the people and on their own profession. It was considered highly desirable to explore the thinking of all the doctors and to bring this thinking into focus on the legislation before these bills come up for action. This was the motivation that resulted in the formation of the Doctors Committee for Improved Federal Medical Services.

Mr. Hoover and Dr. Robert L. Johnson, president of Temple University and chairman of the Citizens Committee for the Hoover Report, asked me to undertake the formation of such a committee. I was glad to do this, because I was concerned about the whole question of Federal medicine and apprehensive over the possible fate of the proposed legislation in the hands of politicians and laymen.

At a meeting in New York we organized the committee and formed an advisory committee of physicians from all parts of the country who represent all the recognized branches of medicine.

With this nucleus we began the recruiting of state chairmen; at present there are 48. They, like the National Doctors Advisory Committee, are made up of a representative group of physicians.

The Doctors Committee for Improved Federal Services is in no sense a policy group. It is nonpolitical, nonpartisan; it requires no fee. It is temporary and was set up solely to find out what the doctors of the country think about the proposed reform of the Federal medical system and to try to bring that thinking to bear on Congressional consideration of the problem. The Committee is not trying to proselytize for the bills. It is not so much concerned with what the doctors think about the subject as that they think and will make their views known to Congress.

Information on this subject is available at the office of the Doctors Committee for Improved Federal Medical Services at 15 West 46th Street, New York 19, New York. There are three steps that the doctors can take in the solution of this national problem.

Become informed and aware of the gross injustices that have been imposed upon the medical profession and the public.

Join the Doctors Committee for Improved Federal Medical Services. Try to stimulate discussion of this problem, and try to interest the medical associations to which you belong to hold open hearings on the subject.

Write your Congressman and the committee members about your opinions and recommendations.

I believe that the doctors of this country now have perhaps their last chance to use their influence in bringing order out of the chaos of Federal medicine. They obviously cannot all go to Washington to attend the hearings on the bills, but they can write.

If the doctors do not co-operate to correct this vital situation and needed reforms are consequently not carried out, they must be prepared to accept part of the blame. Unless the job is done at once by men within the profession, I predict that it will be only a matter of time before the medical profession in this country will find itself in exactly the same predicament as that of the medical profession in Britain — a predicament for which the British medical profession must assume the major responsibility. The recent change in government in Britain will have no effect on the nationalized scheme of medical practice in that country. There is no road back to efficiency and private enterprise. Let us in America keep our ideal of private initiative and efficiency born of private enterprise. Are you doing your part to prevent an era of nationalized medicine here?

30 Rockefeller Plaza

References

1. Meiling, R. L. Changing military medical education in United States *J. A. M. A.* **147**:538-541, 1951.
2. Magnuson, P. B. Personal files.
3. The Commission on Organization of the Executive Branch of the Government. *Appendix O, Federal Medical Service.* Washington: 1949. Pp. 3 and 4.
4. *You and the Hoover Report.* Pamphlet issued May, 1949, by the Citizens Committee for the Hoover Report.
5. Pastore, J. B. Report of Health Resources Advisory Committee, Office of Defense Mobilization. *New York Times,* May 26, 1951.
6. Rusk, H. A. Medicine, mobilization and manpower. *J. A. M. A.* **145**:1256-1260, 1951.
7. Dickinson, F. G. Supply of physicians' services. *J. A. M. A.* **145**: 1260-1264, 1951.
8. Annual Report, Dr. Willard C. Rappleye, Dean, Columbia University's Faculty of Medicine as reported in *New York Times,* July 23, 1951.
9. Reed, L. J. Report of Special Committee for Study of Medical School Grants and Finances. (Sponsored by the United States Public Health Service, 1951.)
10. *Medical Education in the United States.* The National Fund for Medical Education, Incorporated, 535 Fifth Avenue, New York, 1950. P. 23.
11. Dr. Walter B. Martin. Senate Hearings on S. 2008. Pp. 69 and 70.

LIBRARY
MAY 27 1952
MANHATTAN
KANSAS STATE COLLEGE OF AGRICULTURE AND APPLIED SCIENCE

12. *American Legion Magazine.* May, 1951.
13. The Commission on Organization of the Executive Branch of the Government. *Appendix O, Federal Medical Service.* Summary. Herbert Hoover, Chairman. Washington: 1949. Pp. 9-11.
14. Annual V. A. Report, 1950. P. 145.
15. Records of the Research Department of the Citizens Committee for the Hoover Report.
16. Richard L. Meiling, M. D., Chairman, Armed Forces Medical Policy Council. *Annual Report of the Armed Forces Medical Policy Council to the Secretary of Defense.* Washington. June, 1951. P. 76.
17. *New York Times.* July 22, 1951; June 17, 1951.
18. Government services. Air Force: costs cut through medical unification. *J. A. M. A.* **147**:679, 1951.
19. Koontz, A. R. Personal communication.
20. Gerald G. Gross, Editor, WRMS. *Washington Report on the Medical Sciences.* No. 218. August 13, 1951.
21. Personal files of Dr. Paul B. Magnuson, until recently Chief Medical Director, Department of Medicine and Surgery, Veterans Administration.
22. Robert L. L. McCormick, Research Director of the Citizens Committee for the Hoover Report before Senate Labor & Public Welfare Subcommittee. March 12, 1951.
23. *Coronet Magazine.* September, 1951, Vol. 30, No. 5. P. 41.
24. Pamphlet: *Here's How We Can Get Better Federal Medical Services.* New York: Citizens Committee for the Hoover Report. P. 2.
25. *Medical Education in the United States.*[19]
26. The Commission on Organization of the Executive Branch of the Government. *Appendix O, Federal Medical Service.* Summary. Herbert Hoover, Chairman. Washington, 1949. P. 5.
27. Dr. Paul Magnuson before Senate Labor & Public Welfare Subcommittee. February 20, 1951.
28. The Commission on Organization of the Executive Branch of the Government. *Appendix O, Federal Medical Service.* Summary, Herbert Hoover, Chairman. Washington, 1949. P. 19.
29. The Commission on Organization of the Executive Branch of the Government. *Medical Activities.* Herbert Hoover, Chairman. Washington, 1949. P. 15.

PLANNING LOW-SODIUM MEALS: A COMMUNITY PROJECT

PEARL A. THORESON, M.P.H.,* ARTHUR D. BALDWIN, M.D.,† ERNEST M. MORRIS, M.D.,‡ AND WILLIAM J. ZUKEL, M.D.§

NEWTON, MASSACHUSETTS

WITHIN recent years the use of low-sodium diets in the treatment of congestive heart failure has become accepted medical practice.[1] Moreover, the beneficial results obtained in hypertensive patients on the Kempner rice diet have been attributed by some authorities primarily to the rigid sodium restriction of the rice diet.[2] However, attempts to maintain a patient on a rice or other low-sodium diet are often discouraging for both patient and physician; hence often the full potential benefit of the diet is not attained.

A study of low-sodium diets was undertaken in February, 1950, in Newton, Massachusetts, as one of the activities of the joint Heart Demonstration Program of the Newton Health Department and the United States Public Health Service. The purpose of the study was to determine what problems make it difficult for the patient to adhere to a diet low in sodium and what practical solution could correct these difficulties.

The Subcommittee on Nutrition, a group of physicians selected from the staff of Newton–Wellesley Hospital, served as medical advisers to the Heart Demonstration Program nutritionist during this study. Assistance was also provided by the dietary department of Newton–Wellesley Hospital, the Newton Nutrition Center and the Massachusetts Department of Public Health.

STUDY OF PATIENTS' NEEDS

The physicians, nutritionists and dietitians cooperating in the study already had opinions about what was wrong with the rice diet and other low-sodium diets. The rice diet was considered monotonous and intolerable for most patients over a long period of time. Modifications of the rice diet to allow a greater variety of foods were found to be confusing to the patient; they also involved extra expense for low-sodium milk, low-sodium bread and other special preparations. These impressions were confirmed in part by a survey made by the heart-program nutritionist of teaching methods and low-sodium-diet material used in several Boston hospitals. Some diet material from teaching hospitals in other cities was also studied, as well as the diet lists generally available to physicians and hospital dietary departments. Dietary instruction given to cardiac patients in Newton–Wellesley Hospital was also evaluated to obtain further local information.

This background information was valuable, but the advisory committee believed that the study should include information obtained from patients who were trying to follow a prescribed low-sodium diet. To do this, the nutritionist offered to give individual instruction in low-sodium diets to patients in the home, on physician referral. Forty-one patients were referred by their physicians for this study. An initial visit was made to each patient to explain the prescribed low-sodium diet; a follow-up visit was made one week later to determine whether any difficulties were encountered in following the diet and to help to work out these problems with the patients. Additional visits were made when further help appeared necessary.

Some important needs were revealed. It was evident in many cases that the initial instruction given to patients had not been sufficiently practical or complete. Some of the patients had not realized that many of the foods they were accustomed to eating could be included on a low-sodium diet. Many did not know that the diet could be prepared

*Nutritionist, Newton Heart Program, Division of Chronic Disease and Tuberculosis, Public Health Service.
†Chairman, Subcommittee on Nutrition, Cardiac Program Committee of the Newton Heart Program.
‡Director of public health, Newton Health Department.
§Medical officer in charge, Newton Heart Program, Division of Chronic Disease and Tuberculosis, Public Health Service.

with the regular family meals, if their own serving was set aside before salt or other seasoning containing sodium was added to the family's portion. Teaching the use of a wide variety of sodium-free seasonings was also needed to reduce the "flat" taste of the diet.

It was also evident that the diet instruction given to patients needed to be standardized. Diet information given by the physicians, the hospital and the nutritionist, although basically the same, had enough variation to confuse the patients. For example, on a 200-mg. sodium diet, some cereals and vegetable were excluded from one diet list but were permitted on another. The kinds and amounts of meat allowed often varied considerably for a given sodium level. Also, it was found that whole milk was unnecessarily excluded in diets that intended only mild or moderate sodium restriction.

The degree of sodium restriction ordered by some physicians for patients with congestive heart failure was found to vary from unnecessarily severe restriction to ineffectively mild restriction. Caloric levels were at times prescribed very precisely and at other times disregarded entirely. In essence, the study revealed a multiplicity of methods, variation in types and inadequacy of amount of instruction for the patient, often leaving him to follow a monotonous diet of questionable therapeutic effectiveness.

Development of Standardized Diets

Acting on these findings, the Nutrition Subcommittee initiated a community project for developing standardized, nutritionally adequate low-sodium diets. It was hoped that this diet material would fill the need for therapeutic effectiveness yet allow enough variety in the diet to be acceptable to the patient.

As a first step, the heart-program nutritionist, the hospital dietitians and the Newton Nutrition Center nutritionist established average figures for sodium content of five food groups. The five groups were: meats, vegetables, fruits, bread and its exchanges (carbohydrate equivalents) and fats. Sodium values of foods were obtained from analyses reported by Bills and others,[3] using the flame-photometer methods. Finding the average group figure for sodium content consisted of: excluding from each food group all the foods with the highest sodium content; listing the sodium content of average-sized servings of the foods to be included in each group; and calculating the weighted average sodium content of each food group. The weighted average was based on the estimated consumption of the foods in the group. Valuable assistance in determining these figures was provided by the nutrition consultant from the Diabetes Section of the United States Public Health Service. The figures for the composition of the five food groups are shown in Table 1.

Table 1.

Food	Amount		Sodium	Carbohydrate	Protein	Fat	Calcium
		gm.	mg.	gm.	gm.	gm.	
Milk	½ pint	240	125	12	8	10	170
Egg	1	50	40		7	5	73
Meat	1 oz.	30	20		7	5	73
Vegetables	½ cup	100	9	7	2		36
Fruit	Average serving	Varies	2	Approximately 15			60
Bread and its exchanges	Varies	Varies	1	15	2		68
Fats	1 tsp.	5	.25			5	45

The foods included and excluded in each of the above groups are listed in Tables 2, 3, 4, 5 and 6.

Whole milk, evaporated milk and dry skim milk were included on diets of 400 mg. or more of sodium.

Table 2. *Meats.*

Meats Included (Low in Sodium Content)	*Meats Omitted* (High in Sodium Content)
Chicken	Brains
Fish	Clams
Fresh halibut	Crab
Fresh bass	Heart
Fresh cod	Kidney
Fresh oyster	Lobster
Fresh perch	Shrimp
Fresh salmon	Frozen fish to which salt has been added. Any meat, fish or poultry that is smoked, brine cured, canned, salted, dried or salted and soaked (kosher). This includes cold cuts, bacon, ham and sausage. No canned soup of any kind.
Fresh trout	
"Dietetic" tuna	
Lamb	
Chops	
Roast	
Stew	
Lean beef	
Hamburger	
Roast	
Steak	
Stew	
Liver	
Pork	
Chop	
Roast	
Turkey	
Veal	
Chop	
Roast	

Lonalac, dialyzed low-sodium milk, was used on diets of 200 mg. of sodium. The variety of seasonings allowed in the diet and those omitted because of high sodium content are shown in Table 7.

On the basis of current medical practice, the Subcommittee on Nutrition advised that diets be prepared for patients on three sodium levels (200, 400 and 800 mg. of sodium.) For each fixed level of sodium, three caloric levels were calculated (1200, 1500 and 2000 calories). The 200-mg.-sodium diets were planned for use in the treatment of severe or rapidly progressive hypertension; the 400-mg.

sodium diets in treating congestive heart failure; and the 800-mg.-sodium diets for patients in whom less sodium restriction was necessary. The 1200- and 1500-calorie diets were planned to allow weight reduction when needed as part of the treatment. The 2000-calorie diet was planned to be used as a maintenance diet. Nutritional adequacy of the diets was achieved by calculating them according to the National Research Council's "Recommended Daily Dietary Allowances" for sedentary men and women.[4]

TABLE 3. *Vegetables.**

Vegetables Included (Low in Sodium Content)		*Vegetables Omitted* (High in Sodium Content)
Asparagus	Lettuce	Beets
Broccoli	Mushrooms	Beet greens
Brussels sprouts	Onions	Celery
Cabbage	Parsnips	Dandelion greens
Carrots	Fresh peas	Kale
Cauliflower	Pumpkin	Frozen peas
Cucumber	Radishes	Sauerkraut
Eggplant	Squash	Spinach
Endive or chicory	Tomatoes	Swiss chard
Green beans	Turnips	
Green peppers		

*The section on "Bread and Its Exchanges" includes other vegetables allowed.

TABLE 4. *Fruits.*

Fruits Included (Low in Sodium Content)		*Fruits Omitted* (High in Sodium Content)
Apples	Grapes	Raisins
Apricots	Muskmelon	Dried figs
Bananas	Oranges	Canned or frozen fruits with sodium benzoate added
Blackberries	Peaches	
Blueberries	Pears	
Cantaloupe	Pineapples	
Cherries	Plums	
Cranberries	Prunes	
Currants	Raspberries	
Dates	Rhubarb	
Figs	Strawberries	
Gooseberries	Tangerines	
Grapefruit	Watermelon	

TABLE 5. *Bread and Its Exchanges.*

Bread and Its Exchanges Included (Low in Sodium Content)	*Bread and Its Exchanges Omitted* (High in Sodium Content)
Bread (low-sodium)	Regular bread (unless allowed by physician)
Corn	"Quick-cooking" cereals
Hot cereals	Dry cereals not listed
Lima beans	Potato chips
Macaroni	Pretzels
Noodles	Self-rising flour
Plain rice	Salted popcorn
Potatoes	Salted or "soda" crackers
Puffed rice	Salted nuts
Puffed wheat	Other salted foods
Rolls (low-sodium)	
Shredded wheat	
Spaghetti	
Unsalted "Passover" matzoth	

The amounts and kinds of food allowed daily on the 200-, 400- and 800-mg.-sodium diets at the 1500-calorie level are shown in Table 8.

PREPARATION OF BOOKLET

To make the diet information available to patients in an easily understood form, a booklet on planning low-sodium meals was prepared. Opinions on what should be included were obtained from physicians, public-health nurses, schoolteachers, nutritionists, health educators and patients.

The booklet was intended to show that a restricted sodium diet can be appetizing and nutritious. It was written in simple language and contained many illustrations to help the patient understand his diet easily. The text was arranged by food groups, with index tabs for easy reference. Within each group were listed the foods that could be eaten and those that should be omitted. Suggestions to make the meals more palatable, as well as sample recipes, were included. To fill the individual therapeutic diet needs, 9 different diet lists were

TABLE 6. *Fats.*

Fats Included (Low in Sodium Content)	*Fats Omitted* (High in Sodium Content)
Sweet butter	Salted butter
Lard	Oleomargarine
Unsalted vegetable shortenings	Peanut butter
Salad oils (corn oil, olive oil, peanut oil, soybean oil, cottonseed oil)	Bacon drippings
	Commercial mayonnaise
	Commercial French dressing

TABLE 7. *Seasonings and Spices.*

Seasonings and Spices Allowed (Low in Sodium Content)	*Seasonings and Spices Omitted* (High in Sodium Content)
Allspice	Baking soda
Almond extract	Baking powder
Bay leaves	Bouillon cubes
Caraway	Celery salt
Cinnamon	French dressing (commercial)
Cocoa	Garlic salt
Curry powder	Ketchup
Garlic	Mayonnaise (commercial)
Lemon juice	Meat sauces
Marjoram	Molasses
Mustard (dry)	Mustard (prepared)
Nutmeg	Olives
Fresh onion flavoring (juice)	Pickles
Paprika	Salt (plain or iodized)
Parsley	Sugar (brown)
Pepper (black, white, red)	Syrups (commercial)
Pimiento	Worcestershire sauce
Poultry seasoning	
Saccharin	
Sage	
Thyme	
Vanilla extract	
Vinegar	
On some diets, jam, jelly, sugar (white) and honey allowed (no jelly or jam with sodium preservative)	

TABLE 8. *Recommended Daily Food Intake, According to Caloric Level.*

FOOD	DESCRIPTION	AMOUNT OF FOOD		
		1500 CAL. (200 MG. SODIUM)	1500 CAL. (400 MG. SODIUM)	1500 CAL. (800 MG. SODIUM)
Meat	Any in allowed list	4 oz.	4 oz.	5 oz.
Egg		1	1	1
Milk	Fresh, evaporated or powdered	1 pt.	1 pt.	1 pt.
Lonalac	Dialyzed low-sodium milk			
Vegetables	Any in allowed list	2 serv.	2 serv.	2 serv.
Fruit	Any in allowed list	3 serv.	3 serv.	3 serv.
Bread and its exchanges	Any in allowed list	5 serv.	5 serv.	2 serv.
Fats	Any in allowed list	4 tsp.	4 tsp.	4 tsp.
Regular bread				2 slices

prepared. These diets provide three different sodium levels (200 mg., 400 mg. and 800 mg.), each of which is combined with three different caloric levels (1200, 1500 and 2000).

A pocket-size reference card, "Facts and Figures for Physicians," listed the sodium content of commonly used beverages and drugs. The card also gave information on the use of the booklet and included a warning about the possibility of sodium depletion, or "low-salt syndrome," especially when mercurial diuretics are used.

A draft of the booklet was pretested on 30 Newton patients to make certain that it met their needs; their suggestions were helpful. Publication of the booklet was financed by the Newton Health Department.

Use of the Booklet

A major step in the culmination of this attempt to improve low-sodium diets was the publication of the booklet, "Planning Low-Sodium Meals," but it had yet to gain acceptance and use by the physicians of the community.

From the outset, the Nutrition Subcommittee and the Health Department decided that the booklet would be given to patients only on a physician's order. Therefore, the booklet was introduced to physicians at several local medical and staff meetings. The Medical Service and the Dietary Department of Newton–Wellesley Hospital accepted it readily, since their representatives had participated in the development of the booklet. The problem of providing special diets in the hospital has been greatly simplified by this standardization, yet the choice of three levels of sodium restriction allows the physician to satisfy the therapeutic needs of most patients.

The diet instruction received by the patient prior to his discharge from the hospital does not end his need for nutrition services. Patients who return to the out-patient clinics may obtain continued diet instruction as needed. Likewise, the physician may obtain follow-up services by the community nutritionist for his patient in the home. She also uses the booklet as basic teaching material on low-sodium diet. The public-health nurses of the Newton Health Department and of the Newton District Nursing Association have also been instructed in low-sodium-diet interpretation, so that they may give further practical help to patients during home visits.

The problems of obtaining low-sodium diets for patients in nursing homes have largely been eliminated through the adoption of the standardized low-sodium diets by the majority of the nursing homes in the community.

Aside from being used in individual instruction, the booklet has served as a helpful guide in the development of a group education service for patients on low-sodium diets. Low-sodium-diet classes are now being carried on as a further refinement of diet education for patients. Through physician referral, ambulatory patients may enroll for a series of four weekly meetings to obtain information on meal planning, food buying and selecting low-sodium meals in restaurants. Experience with this group education service has been limited, but it seems to fill a need not met by individual instruction. Group instruction makes more efficient use of the nutritionist's time, and, what is more important, the patients seem to benefit from sharing their problems and experiences in following the diet.

Although the materials were prepared for use in Newton, many requests have already been received from teaching hospitals, medical schools, schools of public health, official and voluntary health agencies, physicians and other health workers in 38 states.

Summary

In February, 1950, a group of physicians joined official and voluntary health agencies in Newton, Massachusetts, in a co-operative attempt to overcome some of the problems involved in teaching patients to follow nutritionally adequate low-sodium diets. One result of this co-operative effort was the publication of a diet booklet, "Planning Low-Sodium Meals." The nine diet lists that accompany this booklet allow for three levels of sodium restriction (200, 400 and 800 mg.) and three caloric levels (1200, 1500 and 2000 calories) for each sodium level. A system of "weighted" values of different foods according to their sodium and caloric content permits the use of food exchanges, giving the patient a wide choice in planning meals.

It is recognized that the development of diet information using group figures for sodium content has scientific limitations, since there are variations in the sodium analyses reported by different investigators. However, the advantages of this approach have already been demonstrated by the favorable reports on the use of the booklet by both physicians and patients in the community of Newton and elsewhere.

Acceptance of this standardized diet material by physicians and patients has led to a nearly uniform approach to low-sodium-diet education throughout the community. Individual and group diet-education services for patients on low-sodium diets have been another outgrowth of this project.

The results of this attempt to improve low-sodium diets are presented in the hope that they will help physicians to extend the therapeutic benefits of low-sodium diets more effectively to patients for whom they are indicated.

References

1. Harrison, T. R., and Resnick, W. H. The cardiovascular system. In *Principles of Internal Medicine.* Edited by T. R. Harrison et al. 1590 pp. Philadelphia: The Blakiston Company, 1950.
2. Corcoran, A. C., Taylor, R. D., and Page, I. H. Controlled observations on effect of low sodium dietotherapy in essential hypertension. *Circulation* 3:1-16, 1951.
3. Bills, C. E., McDonald, F. G., Niedermeier, W., and Schwartz, M. C. Sodium and potassium in foods and waters. *J. A. Dietet. A.* 25:301-314, 1949.
4. National Research Council. *Recommended Dietary Allowances* (Revised 1948). Food and Nutrition Board, 2101 Constitution Avenue Washington 25, D. C.

THE RELIABILITY OF THE L. E. TEST*

JOHN R. WALSH, M.D.,† AND RICHARD L. EGAN, M.D.‡

OMAHA, NEBRASKA

IN JANUARY, 1948, Hargraves, Richmond and Morton[1] announced the discovery of a cell in bone-marrow preparations from patients with disseminated lupus erythematosus that they called the L. E. cell. It was soon demonstrated that the factor producing this phenomenon was in the plasma.[2-4] When plasma from patients with disseminated lupus erythematosus is added to normal bone marrow the L. E. cell appears. Further studies identified gamma globulin as the fraction of the plasma responsible for this phenomenon.[5] From these experiments the L. E. plasma test evolved and has been widely used in the diagnosis of systemic lupus erythematosus.

If the L. E. plasma test is as reliable as originally assumed, it would permit an earlier and more accurate diagnosis of systemic lupus erythematosus.

TABLE 1. *Results in Patients Tested for L. E. Phenomena.*

No. of Cases	Diagnosis	Results
3	Rheumatic fever	Negative
5	Rheumatoid arthritis	Negative
1	Periarteritis nodosa	Negative
5	Discoid lupus erythematosus	Negative
1	Nephritis	Negative
1	Multiple myeloma	Negative
1	Erysipelas	Negative
1	Chronic eczematoid dermatitis	Negative
2	Contact dermatitis	Negative
1	Normal	Negative
4	Systemic lupus erythematosus	Positive

Lee, Michael and Vural[6] have reported a cell identical in appearance with the L. E. cell in a case of primary amyloidosis. The occurrence of L. E. cells in a case of multiple myeloma and in leukemia has been reported.[7] Likewise, Berman and others[8] have reported finding L. E. cells in six patients who could not be said to have disseminated lupus erythematosus. They recommended that a ratio of more than 10 L. E. cells to 500 neutrophils be considered a positive test for the presence of systemic lupus erythematosus.

METHOD

This study was undertaken to determine the specificity of the plasma L. E. phenomenon for systemic lupus erythematosus. The procedure of Haserick and Bortz[4] for demonstration of the L. E. phenomenon was followed. Of the 25 patients whose plasma was tested, 4 represented systemic lupus erythematosus, 5 had the discoid variety of lupus erythematosus and the remainder included a number of miscellaneous diseases (Table 1). A positive test consisted in the demonstration of typical L. E. cells and clumping of polymorphonuclear leukocytes in rosette arrangement (Figure 1). Using the same concentration technic, the normal bone-marrow specimens employed in these procedures were studied to verify their normalcy. Plasma yielding positive results when tested with one marrow sample was checked with marrows obtained from several normal persons.

FIGURE 1.

Of the group of diseases studied, the test was positive only in the 4 patients with systemic lupus erythematosus. Plasma from each of these patients produced consistently positive tests in 2 to 7 different marrows.

Plasma from patients with rheumatic fever, rheumatoid arthritis and periarteritis nodosa failed to produce the L. E. phenomenon when added to normal marrow. Patients with rheumatoid arthritis in stages of the disease varying from recent acute to chronic likewise failed to give a positive test.

DISCUSSION

Differentiation or even recognition of the collagen group of diseases is frequently difficult without the aid of laboratory procedures. The authors believe

*From the Department of Medicine, Creighton University School of Medicine.

†Assistant in medicine, Creighton University School of Medicine.

‡Assistant professor of medicine, Creighton University School of Medicine.

that the most important laboratory complement for distinguishing lupus erythematosus is the L. E. factor test. It was observed that the usual findings of typical butterfly rash, leukopenia, increased plasma globulin and false positive serology frequently associated with systemic lupus erythematosus were not always present in our patients. All 4 patients with systemic lupus erythematosus showed a positive L. E. test. In the group of 25 patients studied there were no false positive tests; this agrees with the reports of Suksta and Conley[9] and of Haserick.[10]

Intensive cortisone therapy of systemic lupus erythematosus did not change significantly the results of the test. Although this has been the experience of most investigators, some authors state that the number of L. E. cells is diminished after cortisone or corticotrophin therapy.[11]

The possibility of using the number of L. E. cells seen in a smear as a prognostic aid has been suggested by Haserick.[10] Observations made on one of our patients who died while on cortisone therapy were in keeping with this impression. In this particular case, the L. E. plasma test was strongly positive and revealed a much greater number of L. E. cells than preparations from less fulminating cases.

Summary

It was the purpose of this investigation to determine the reliability of the L. E. factor test for systemic lupus erythematosus. A number of cases from the collagen group of diseases were examined, namely, rheumatic fever, rheumatoid arthritis, periarteritis nodosa and systemic lupus erythematosus. Of this group only cases of systemic lupus erythematosus gave positive results. Discoid lupus erythematosus gave consistently negative results. There was, however, no opportunity to evaluate the reliability of this test in patients experiencing acute exacerbations of this disorder. Plasma from cases of multiple myeloma, nephritis, erysipelas, contact dermatitis and chronic eczematoid dermatitis gave negative results. The results obtained in this study substantiate the reliability of the L. E. test in the diagnosis of systemic lupus erythematosus.

References

1. Hargraves, M. M., Richmond, H., and Morton, R. Presentation of 2 bone marrow elements: "tart" cell and "L. E." cell. *Proc. Staff Meet., Mayo Clin.* **23**:25-28, 1948.
2. Hargraves, M. M. Production in vitro of L. E. cell phenomenon: use of normal bone marrow elements and blood plasma from patients with acute disseminated lupus erythematosus. *Proc. Staff Meet., Mayo Clin.* **24**:234-237, 1949.
3. Haserick, J. R., and Bortz, D. W. Normal bone marrow inclusion phenomena induced by lupus erythematosus plasma. *J. Invest. Dermat.* **13**:47-49, 1949.
4. *Idem.* New diagnostic test for acute disseminated lupus erythematosus. *Cleveland Clin. Quart.* **16**:158-161, 1949.
5. Haserick, J. R., Lewis, L. A., and Bortz, D. W. Blood factor in acute disseminated lupus erythematosus: determination of gamma globulin as specific plasma fraction. *Am. J. M. Sc.* **219**:660-663, 1950.
6. Lee, S. L., Michael, S. R., and Vural, I. L. E. (lupus erythematosus) cell. *Am. J. Med.* **10**:446-451, 1951.
7. Fisher, G. S., and Moyer, J. B. Hematologic phenomena as test for acute disseminated lupus erythematosus. *Grace Hosp. Bull.* **28**: 3-9, 1950.
8. Berman, L., Axelrod, A. R., Goodman, H. L., and McClaughry, R. I. So-called "lupus erythematosus inclusion phenomenon" of bone marrow and blood: morphologic and serologic studies. *Am. J. Clin. Path.* **20**:403-418, 1950.
9. Suksta, A., and Conley, C. L. Some observations on L. E. cell. *J. Lab. & Clin. Med.* **37**:597-602, 1951.
10. Haserick, J. R. Plasma L. E. test in systemic lupus erythematosus: study of twenty-three patients with positive L. E. tests. *J. A. M. A.* **146**:16-20, 1951.
11. Soffer, L. J., Levitt, M. F., and Baehr, G. Use of cortisone and adrenocorticotropic hormone in acute disseminated lupus erythematosus. *Arch. Int. Med.* **86**:558-573, 1950.

MEDICAL PROGRESS

EXAMPLE OF THE ACUTE RADIATION SYNDROME IN MAN*

L. H. Hempelmann, M.D.†

ROCHESTER, NEW YORK

THE acute radiation syndrome is an illness produced by exposure of the entire body, or a large part of the body, to ionizing radiations of a penetrating character. Although virtually unknown in clinical medicine before the close of the last war, it is now a type of injury with which the practicing physician must become acquainted. Many reports have described the clinical syndrome as it was observed in the Japanese injured by radiation in the atomic explosions in 1945. The few cases of acute radiation injury that have occurred in this country have only recently been recorded in the open medical literature.[1, 2] Because of the widespread interest in illness of this nature, the present paper presents an abstract of the case histories of three persons of a group injured by ionizing radiation. These cases, which have been described in detail in the articles referred to above, are taken from the files of the Los Alamos Scientific Laboratory and the Los Alamos Hospital.

The clinical manifestations of the acute radiation syndrome differ in many respects from those of body injury caused by the usual physical traumatic agents. Also, they are unlike the types of radiation damage encountered in medical practice and previously described in medical literature. Thus, most cases of the acute radiation syndrome have little in common with acute radiation burns of the skin or insidiously developing chronic radiodermatitis and aplastic anemia. In many ways the clinical picture of the acute radiation syndrome resembles a

*From the Division of Experimental Radiology, University of Rochester School of Medicine and Dentistry.

chemical poisoning or an infectious disease. It is similar in many respects to agranulocytosis from any cause.

The reasons for the unusual clinical manifestations seen in acute radiation injuries become apparent when one considers the manner in which ionizing radiation produces tissue damage. The biologic mechanisms involved are known to all radiologists and to most physicians. A brief review of certain characteristics of radiation, however, is helpful in explaining the clinical and pathological findings in the present cases.

Ionizing radiations have three characteristics of interest to the present study. These are: their ability to penetrate matter (including tissue), the selective damage that they produce in certain organ systems and the delay in the manifestation of tissue damage.

The ability of ionizing radiation to penetrate tissue is utilized in the fields of diagnostic radiology. It is not a universal characteristic of all ionizing radiations; alpha rays, beta rays and very soft x-rays have only limited powers of tissue penetration. However, the more penetrating radiations (hard x-rays, gamma rays and fast neutrons) can reach and directly damage any organ in the body. In this three-dimensional quality, the injuries produced by these ionizing radiations differ from those caused by heat and ultraviolet radiation.

All tissues exposed to ionizing radiation are not affected equally. Radiation therapy capitalizes on the differential damage produced in malignant and normal tissues by x-rays and radium. A comparable differential in radiosensitivity exists among different normal tissues of the body. For the most part, the radiosensitive tissues are those that proliferate rapidly, such as the blood-forming organs and the intestinal and germinal epithelium. In contrast, the nongrowing or slowly growing tissues, such as liver and nerve cells, are usually radioresistant.

Unlike thermal burns, which cause immediate death of tissue, radiation injuries (except for those produced by very high doses) do not become manifest for some time after exposure. An example of this is an x-ray reaction of the skin. Here, the development of epidermolysis may be delayed for a week or so after irradiation of the skin with a large dose of x-rays. The latent period between exposure and the appearance of tissue damage varies from one tissue to another. Thus, in contrast to the slowly developing epidermolysis, death of tissue lymphocytes in an irradiated person occurs within an hour after irradiation. The lymphopenia that develops promptly after exposure to ionizing radiation is a consequence of this.

These unique aspects of the injury caused by exposure to ionizing radiation explain the clinical picture seen in acute radiation injury. Thus, radiation produces tissue damage and death in the more radiosensitive organs of the body. This damage does not become manifest immediately but is delayed after exposure for a period of time that varies with each organ system. The clinical manifestations in a person injured by ionizing radiation are the consequence of tissue damage, the response of the body to this damage and factors, such as infection and fluid loss, that are secondary to tissue damage.

The severity of the illness in a person injured by ionizing radiation depends largely on the dose of radiation and the amount and location of the tissue damage. It must be emphasized, however, that there is a great difference in the responses of persons exposed to the same dose of radiation. Animal experiments have shown that some individuals of a species can survive more than twice the dose of radiation that will cause death in the most sensitive members of the same species. Such variability is analogous to the individual variations encountered in the use of drugs.

The radiation injuries described herein* were a consequence of two nuclear-fission reactions that occurred inadvertently in 1945 and 1946. The chain reactions that took place in experimental assemblies composed of fissionable materials were identical to that which occurs in an atomic explosion. However, they were stopped before a clinically significant amount of energy was released in the form of heat or explosive forces. The radiations given off during the brief interval when the reaction was uncontrolled caused the death of 2 persons and exposed 8 others to varying doses.

The radiation that caused bodily damage was a mixture of neutrons, gamma rays, beta rays and soft x-rays. The calculated radiation doses to which the patients were subjected are given in each case history. The details of the dose computations are beyond the scope of this article but have been published separately.[1] Neutrons and gamma rays, — particularly the former, — accounted for most of the bodily injury. Beta rays and soft x-rays added to the tissue damage, particularly on the hands in Case 1 and the uncovered parts of the body in Case 4. The gamma rays, which were very penetrating, uniformly irradiated the tissues of the body. The gamma-ray doses, expressed in terms of roentgens, can be appreciated by comparing them with the gamma rays from radium or the x-rays from supervoltage x-ray machines (million-volt or more). Unlike the gamma rays, the neutrons were only slightly more penetrating than the soft x-rays from the superficial-x-ray machines used to treat cancer of the skin. This means that the direct tissue damage caused by the neutrons was confined largely to the superficial few inches of flesh nearest the nuclear reaction. The neutron exposures are expressed in terms of the number of roentgens of 80-kv x-rays

*A total of 10 persons were exposed to total body radiation as a result of two nuclear accidents in 1945 and 1946. Two were fatally injured, 2 had symptoms of severe body injury and the remaining 6 had no symptoms of any sort attributable to radiation injury.

that would have produced the same amount of tissue damage.*

It is interesting to compare these radiation doses with those used in x-ray therapy. Before quantitative comparisons between the exposures in these cases and that used in therapy can be made, two important differences in the exposure conditions should be emphasized. In the first place, when x-rays are used to treat a deeply placed neoplasm, only a limited part of the body is irradiated. For example, a beam of 220-kv x-rays measuring 10 by 10 cm. may be directed at the tumor through several portals. As a result of this treatment, only a portion of the body, about 1/10th or less, is irradiated. In the present cases, the entire body was exposed to radiation. Thus, more tissue was irradiated in the present cases than in the usual patient

FIGURE 1. *Case 1: Dorsal View of Both Hands Three and One-Half Days after Exposure, Showing Blisters Tensely Distended with Fluid. (Reproduced from Hempelmann, Lisco and Hoffman[2] by Permission of the Publisher.)*

under x-ray treatment. Therefore, a greater constitutional reaction is to be expected in persons whose entire body was irradiated than would be caused by the same radiation dose delivered to a small part of the body. This is analogous to the extensive or limited thermal burns that may be produced by exposing varying amounts of skin to the same heat intensity (calories per gm.). Secondly, in x-ray therapy, treatments are given daily or every other day for a period of a month or so. The protraction of the total radiation dose allows the irradiated tissues to recover somewhat between treatments. In the patients discussed in this article, the radiation was delivered in a fraction of a second; thus the full impact of the radiation was suffered at the time of the accidents.

With these differences in exposure conditions clearly in mind, let us consider the radiation doses used in cancer therapy and those received by these patients. In the treatment of an internally placed cancer, such as a bronchiogenic carcinoma, 4500 r† of penetrating x-rays may be delivered to the thorax through six portals, each 10 by 10 cm. This course of treatment will last four to five weeks. The x-ray beams converge in the body and intersect in the tumor-containing region. These tissues, weighing perhaps 500 gm., may receive 6000 r. In Case 1, the radiation dose consisted of soft radiation (moderately fast neutrons) equivalent to about 490 r of soft x-rays and of extremely penetrating radiation (gamma rays) equal to about 100 r. This was delivered instantaneously to the entire body. It should be emphasized that this is the *average* dose received by the body. Actually, the radiation dose was not uniform, and the hands and abdomen received much more than this average dose. In addition, the hands were exposed to an additional large dose of very soft radiation equivalent to many thousand r of very soft x-rays.

The following are abstracts of three case histories of persons injured by radiation as a result of accidental nuclear reactions at the Los Alamos Scientific Laboratory.

CASE 1. A 26-year-old man was brought to the hospital 25 minutes after the accident. He was working with a large amount of fissionable material when the chain reaction took place. He actually touched the material; hence he received a very large dose of radiation, especially to his right hand and arm. It has been calculated that his entire body received a radiation dose equivalent to 490 r of 80-kv x-rays and 100 r of gamma radiations. As has been pointed out, the radiation dosage was unevenly distributed over his body; his hands and abdomen received much more than this average dose. The right hand probably received the equivalent of 20,000 to 40,000 r of soft x-rays.

Examination on admission revealed a heavy-set, moderately obese young man in good physical condition. His only subjective complaint was numbness and tingling of both hands. The skin of the forearms, neck and face was reddened as a result of sunburn received two days previously. Examination of the heart and other organ systems indicated no abnormalities. The significant physical findings on admission were limited to the hands. The right hand was diffusely and tensely swollen. The skin of this hand was pallid but warm. There was some swelling of the index finger and swelling of the left hand, with suggestion of redness on the grasping surface of the terminal phalanges of these fingers. The oral temperature was 99°F.; the respirations were 20; the pulse was 68 and the blood pressure 120/70.

He was known to have a cardiac abnormality, first discovered 3 years previously. It had later been diagnosed as Wolff–Parkinson–White syndrome. His blood pressure had always been normal; his heart was not enlarged to percussion or x-ray examination. His exposure to radiation had been irregular and not in excess of the maximum permissible dose. Blood counts and urinalysis had been normal.

Within 30 minutes after admission both his hands were swollen with a brawny edema. One and one-half hours after exposure he had severe gastric distress manifested by nausea and repeated episodes of retching and vomiting. At times this was almost continuous. These symptoms lasted intermittently throughout the first 24 hours after the accident. During the second day nausea persisted. The patient no longer vomited, but he suffered from prolonged periods of hiccoughing. There was no diarrhea or distention. The swelling of the hands increased rapidly during the first 2 days, spreading to involve almost the entire extremities. The edema was more pronounced on the right hand. Numbness in both hands was replaced by gradually increasing pain,

*The conversion of neutron doses into the equivalent x-ray exposures involves assumptions that make the computed doses arbitrary in certain respects. (This is fully discussed in Reference 2.)

†This is the dose measured at the surface of the body.

which became the outstanding symptom during the first week. It was also noted that he was dyspneic on slight exertion such as sitting up in bed. From the 3rd to the 6th day he felt relatively well.

On the 6th day toxicity developed and became worse daily. On the 10th day a "canker sore" was noted on his tongue. He became nauseated after eating on this day. Cramps and generalized abdominal pain appeared, accompanied by distention and tenderness in the right upper quadrant. A generalized stomatitis developed, involving all the mucous membranes of the mouth. A thick gray-white membrane covered the entire oral mucosa and edges of the tongue. The lips were bleeding, swollen and cracked. The mouth became extremely sore. The patient refused food and drink. It was necessary to give him fluids parenterally for several days. In addition to stomatitis, there was moderate paralytic ileus and diarrhea.

FIGURE 2. *Case 1: Palmar View of the Right Hand Nine Days after Exposure.*

The epidermis has been cut away. There was no blanching of the dermis of the palm on pressure. The fingers were cold to the touch. No radial pulsation could be felt. (Reproduced from Hempelmann, Lisco and Hoffman[2] by permission of the publisher.)

Stomatitis subsided gradually, leaving small ulcerative lesions on the floor of the mouth by the 18th day but reappeared terminally as necrotizing ulceration. He passed liquid stools on the 12th day and from this time on frequently passed soft and poorly formed stools. After intravenous medication on the 15th day he had an attack of paroxysmal auricular tachycardia that lasted 24 hours. Electrocardiographic study showed a nodal rhythm after the tachycardia had ceased. Clinical signs of pericarditis were noted on the 17th day.

In addition to severe toxic systemic reaction, there was a progressive development of localized tissue injury in both extremities and on the abdomen. This inflammatory reaction reached its maximum during the 2nd week after the accident. The right hand began to blister 36 hours after exposure. The left hand, having been less heavily exposed, did not blister until the 11th post-exposure day. This process spread until almost all the skin of the right forearm and that of the distal half of the left forearm had been lost by the time of death. In the beginning the denuded surfaces exuded large quantities of yellow fluid. During the second week the tissue became progressively less moist, finally progressing to dry gangrene of the fingers of the right hand and of the thumb of the left hand. The skin of the patient's abdomen became erythematous on the third day and began to blister on the 17th day. All the epidermis of the abdomen and lower chest was lost by the time of death. The reaction was most severe and painful in the groin, where considerable maceration of the tissue occurred. The hair of the temple and beard started to epilate on the 19th day. Loss of hair was almost complete at the time of death.

In the course of the illness the patient's condition deteriorated steadily. He lost much weight, and his appearance changed markedly. There were occasional periods of mental confusion in the early stages of the illness. The sensorium remained alert and normal, however, until several days before death, when the patient became irrational. He became comatose on the 24th day and died in the afternoon of that day.

Blood counts made prior to the accident had always been normal. The total leukocyte count varied between 6000 and 9200, with a normal differential. Blood counts were taken twice daily after the accident. The main changes in the leukocyte count were: two periods of granulocytosis, one lasting from the accident to the 7th day, the other from the 15th to the 18th day; a prompt and persistent lymphopenia; and terminal and pronounced fall of all leukocyte types. The platelet count fell moderately during the period between the waves of granulocytosis and again in the period before death. There was a gradual fall in the red-cell count and the hemoglobin. The urine showed faint traces of albumin on the 10th and 18th days, and stools were guaiac positive on the 10th, 12th and 16th days. There was no evidence of kidney damage. A measurable amount of radioactivity (chiefly sodium and phosphorus) was detected in the blood serum and the urine.

Treatment was largely symptomatic. The injured hands were initially chilled by means of ice packs. Paravertebral block on the right side was performed on the third day in an attempt to improve the circulation. The burns on the hands were treated as thermal burns with surgical débridement and pressure dressings. The hands were redressed every 3 or 4 days and the wounds débrided so that progress of the lesion might be observed. Tachycardia was treated with quinidine sulfate, 0.4 gm. every 4 hours, orally. Intramuscular injections of penicillin (25,000 units) were given every 3 hours after the 6th day. Codeine and morphine were administered for pain as needed. The patient was placed on a nutritious bland diet with supplementary vitamins including 30 mg. of thiamin chloride (intramuscularly) per day. The daily intake of fluid was kept above 3000 cc. During the period of gastrointestinal distress and terminally it was necessary to give fluids parenterally. Two pints of blood was administered on the 14th and 15th days. Intravenous therapy was not employed after this time, because of the risk of precipitating an attack of tachycardia.

FIGURE 3. *Case 1: Palmar View of the Right Hand Twenty-Four Days after Exposure.*

The contraction of the fingers is evident. The tissues of the palm and wrist were pale in color as a result of ischemia and necrosis. (Reproduced from Hempelmann, Lisco and Hoffman[2] by permission of the publisher.)

Post-mortem examination showed extensive burns involving the hands, forearms and the anterior portion of the midsection of the torso and loss of hair in the bearded area and on the anterior part of the scalp. There was advanced dry

gangrene of all fingers of the right hand and of the left thumb. There were several ulcers in the buccal mucosa; the skin was yellow. The thoracic organs revealed an extensive serofibrinous exudate covering the pericardium of the hypertrophied heart as well as moderate edema in the dependent portions of the lungs. The pericardial reaction was most striking over the left ventricle, where the thick exudate was hemorrhagic. The abdominal organs showed moderate enlargement and flabbiness of the liver and spleen. There was marked atrophy of the Malpighian bodies, as visualized on the cut surface of the spleen. The intestine showed marked injection over segments of the ileum and a solitary ulcer in the transverse colon. There were two ischemic infarcts in the right kidney; the testes showed a decrease in size. The adrenal glands were of normal size and appearance. The most obvious change in the appearance of the blood-forming tissue was the watery consistency of the red marrow. Although many lymph nodes were somewhat smaller than normal, those in the axillary and inguinal groups were swollen. The blood was clotted in apparently normal fashion at the time of autopsy.

FIGURE 4. *Case 1: View of the Left Hand Fifteen Days after Exposure, Showing the Blister that Involved the Palm, Thumb and Forearm.*

The forearm is less swollen than previously. (Reproduced from Hemplemann, Lisco and Hoffman[2] by permission of the publisher.)

The illness of this patient illustrates the clinical course produced by exposure of the entire body to ionizing radiation. The syndrome can be broken down into four phases: an initial reaction lasting a day or so after exposure; a period of relative well-being; a febrile or toxic phase; and either death or eventual recovery. The initial reaction occurs promptly after exposure and is characterized by prostration, nausea and vomiting and sometimes by diarrhea. The improvement during the second phase is often striking, but the patient usually does not recover completely. This is illustrated by the weakness and exertional dyspnea noted in this patient. The clinical manifestations of the third or toxic phase include fever, loss of weight, oropharyngeal ulcerations, diarrhea and agranulocytosis. Unlike Patient 1, most persons bleed from the mucous membranes or into the skin during this phase. Cardiac arrhythmia has not been reported in other such cases; it presumably represents an individualized response in this patient, who had a congenital cardiac defect. Death, often associated with infection, usually occurs within six to eight weeks after exposure.

The immediate reaction of the hand tissues noted in this case was probably due to the exceedingly large amount of the radiation dose. It is not observed in the usual case of total body radiation damage such as was noted in the Japanese. Treatment of these lesions posed a new problem, as the extent of the damage was not appreciated early in the illness of this patient. The use of pressure dressings, frequently changed so that the progress of the lesions might be followed, was patterned after the treatment of thermal burns. In a subsequent fatally injured patient with comparable damage to the tissues of the hand the irreversible nature of the destructive process was realized early in the illness and the hands were packed in cracked ice. This was effective in controlling pain and probably diminished the release of toxic products of tissue breakdown into the general circulation. Therapy of the acute constitutional reaction was entirely symptomatic — antiobiotics to prevent or counteract infection, transfusions to replace the formed elements of the blood, maintenance of the fluid and electrolyte balance and good nursing care. Intravenous therapy, including transfusions, was used with caution in this patient after the tachycardia on the 15th day, due to the risk of precipitating an attack of cardiac arrhythmia.

CASE 2. A 34-year-old man was brought to the hospital within 1 hour after the accident. He was 3 feet away from the experimental assembly and was turned slightly to the left when the nuclear reaction occurred; the radiation entered the left anterior side of the body. The radiation dose delivered to his body is estimated to be equivalent to 390 r of soft x-rays and 26.4 r of gamma rays. He was partially shielded from the radiations given off during the reaction; his head, shoulders and left arm received a greater dose than the rest of the torso.

He had been in good health prior to the accident. He was known to have a mild hypertension and to show intermittent albuminuria. He was married and had 1 child. He had worked with ionizing radiation for several years. His exposures were intermittent and were known to be well below 0.1 r per day, except on two occasions when he received several r in 1 week. He had not been exposed to radiation for 18 months previously.

Examination on admission showed him to be in good condition. There was a slightly elevated diastolic pressure (136/96). The heart was not enlarged to percussion. No skin lesions were present. The oral temperature was 99.4°F., the pulse 100 and the respirations 20. He was calm and had no subjective complaints.

Several hours later he vomited once. The nausea disappeared in the next 12 hours, and his appetite returned. There was no diarrhea or other evidence of gastrointestinal disturbance. Fourteen hours after exposure his blood pressure fell to 120/80. It remained at this level for 24 hours and then returned to the pre-exposure level of 140/90. For several days he felt weak and tired and appeared prostrated but was otherwise asymptomatic. On the fifth day his temperature rose slightly; by the 6th day it had reached 102.6°F. He now complained of drowsiness, anorexia and constipation. His face was flushed. His abdomen was soft and nontender. Penicillin therapy was instituted at this time in view of the possibility that the signs and symptoms were due to infection. The temperature gradually fell to normal by the 10th day, and his condition improved. His appetite returned and he

LIBRARY MAY 27 1952 MANHATTAN KANSAS STATE COLLEGE OF AGRICULTURE AND APPLIED SCIENCE

felt much stronger. His only remaining complaint was epistaxis on blowing his nose. Cauterization of both nares resulted in prompt cessation of nasal bleeding. Almost complete disappearance of occult blood in the stool was noted after this procedure. There were no gastrointestinal symptoms at this time. Proctoscopic examination on the 10th day revealed completely normal epithelium, rectum and lower sigmoid colon. His strength steadily improved; he was allowed out of bed several hours a day after the 10th day, without untoward reaction.

On the 15th day the patient was discharged from the hospital with instructions to rest at home for several weeks. He felt well, except for some residual weakness and fatigability. Physical examination showed no change except for a weight loss of 10 pounds.

FIGURE 5. *Case 1: Right Side of the Head Twenty Days after Exposure, Showing Loss of Beard and Hair on the Temple. The naevus on the cheek was slightly smaller than before. (Reproduced from Hempleman, Lisco and Hoffman[2] by permission of the publisher.)*

His treatment in the hospital was symptomatic — complete bed rest for 10 days and penicillin, 50,000 units, intramuscular every 3 hours from the 5th through the 8th day. At this time it was stopped because of an urticarial reaction. His fluid intake was kept above 2500 cc. per day. He was given 500 cc. of lyophilized plasma on the 1st and 3rd days, two 500-cc. blood transfusions on the 3rd and 4th days and several liters of intravenous fluids when fluid intake by mouth was diminished.

The mild increase in activity following discharge from the hospital was tolerated poorly by the patient. He tired easily after mild exercise and required 16 hours of bed rest daily. During the first week after discharge from the hospital he used more salt on his food than usual. On the day of discharge from the hospital his skin was clear, but he complained of dryness of the skin over the forehead, left hand and groin. He also noted dryness of the mouth. There was numbness and some loss of tactile sensation of the skin of the left hand and forearm. This persisted for about 10 days. The sensation of the skin of the left hand and forearm returned slowly. The sensation of dryness of the skin and mouth gradually disappeared. Some desquamation of the skin of the hand and feet was observed 1 month after exposure. At this time the skin of the right hand appeared more flushed than that of the left. The redness gradually turned to a tan that persisted for several weeks. Three months after exposure, ridging of the left fingernails was observed. The nails of the right hand showed no change. On the 17th day after exposure, the patient noted a localized area of tenderness of the skin of the left temple. This tenderness increased over a two-day period until the act of touching the hair of this region caused pain. The hair began to epilate on the left temple and beard. The eyebrows were not affected, but there was temporary diminution of the body and pubic hair.

There was a gradual return of strength and weight. By the end of the 6th week after exposure the patient's weight had returned to normal, and he was able to take a 1-mile walk without fatigue. Approximately 10 weeks after exposure his strength and endurance were back to normal, and he returned to work. Regrowth of hair was complete 4 to 5 months after exposure. Since this time he has led an entirely normal life, working hard and engaging in outdoor sports. During the 28-month period following the accident, repeated seminal-fluid examinations and two testicular biopsies indicated radiation sterility. There was no change of libido or secondary

FIGURE 6. *Case 4: Epilation of Left Temple Two Months after Exposure. Note that the blond eyebrows are still present. The diminution in growth of beard on the left side of the face is evident. (Reproduced from Hempelmann, Lisco and Hoffman[2] by permission of the publisher.)*

characteristics. During the second year after exposure, the patient believed that the testes were smaller and located higher in the scrotum. A surgeon stated at the time of the first testicular biopsy (8 months after exposure) that the testes were softer than normal.

Twenty-eight months after the accident, the only evidence of injury was a diminished sperm count. Thirty-two months after the accident, examination of the patient's eyes showed an indistinct haziness of the posterior cortex of the left lens. He felt well 38 months after exposure. He was working extremely hard in a position of great responsibility. He was taking moderately strenuous physical exercise, including skiing at high altitudes. At this time, however, he had a moderately advanced radiation cataract in the posterior third of the lens cortex, with disk-like opacity of the left lens. There was also diminished visual acuity (20/40) of this eye.

All other laboratory tests, including liver, kidney-function and blood studies, were within normal limits. The patient became the father of a normal son 5 years after the accident.

Laboratory studies of the blood made on the first day revealed a high white-cell count. For several days thereafter, it fluctuated between normal and high. Granulopenia developed on the 5th day. There was a temporary rise in the white-cell count between the 8th and 18th days; the granulocyte count had gradually risen to normal by the end of the second month. In contrast, the lymphocyte count fell much more promptly and remained low for over a year. The platelet count dropped to 100,000 and remained low for 10 days. The erythrocyte and hemoglobin levels decreased gradually, resulting in a very mild macrocytic hyperchromic anemia, most marked between the 40th and 70th days after exposure. Repeated urinalyses showed no indication of kidney damage. Radioactivity of the urine and serum sodium and urine phosphorus was detected shortly after exposure. Sperm and testicle biopsies disclosed a state of complete but transient sterility from which the patient appeared to be recovering 26 months after exposure. Four and a half years after irradiation his sperm count was 16,000,000 per cu. mm.

This case illustrates sublethal acute radiation injury. The most important lesson to be learned from the study of this case is that the toxic phase that follows the period of relative well-being may delayed for several weeks. Such delayed reactions were common among the Japanese. Persons exposed to a large dose of total body radiation should be considered to be potentially injured for at least one month. Physical activity must be limited after such an exposure. The late development of cataracts, the temporary sterility, the prompt lymphopenia and the transient fall in platelets are well known consequences of exposure of the body to radiation. The radioactivity in the sodium and phosphorus of the body is a result of absorption of the neutrons by these tissue atoms. The amount of radioactivity, although measurable, was small and did not constitute a radiation hazard either to the patient or to persons nearby.

This case also shows the extent to which recovery can occur from acute exposure to ionizing radiation. Despite signs of severe acute injury occurring soon after injury, this patient has been able to return to a useful and vigorous life and appears normal except for the cataract, which is not serious enough to warrant surgical removal of the damaged lens.

Case 3. A 54-year-old unmarried man was admitted to the hospital 1 hour after exposure. He was standing six feet from the assembly at the time of the accident. His body received a uniformly distributed radiation dose equivalent to 186 r of soft x-rays and 10.7 r of gamma rays. His only symptom on admission to the hospital was a flushed sensation of his face. Physical findings on admission and during the period of hospitalization were entirely normal. He was in excellent physical condition. His blood pressure was 125/80. He was partly bald. His skin was bronzed from exposure to the sun. There was a moderately severe gingivitis.

His past history was irrelevant. He was in the best of health and had always been physically active. He was in the habit of taking 20- to 40-mile hikes each weekend. There was no history of previous exposure to ionizing radiation or toxic chemicals. Repeated blood counts and urinalyses were normal.

He felt entirely well during the 2-week period of hospitalization. His blood pressure did not fall during the 1st day. He had no fever. His appetite was good. There was no nausea vomiting or diarrhea. There were no symptoms referable to the intestinal tract; proctoscopy on the 10th day revealed normal intestinal mucosa. Erythema, petechial hemorrhages or icterus was not present. His weight did not change. There was no epilation or loosening of the hair of the scalp. He did not complain of fatigability or weakness after leaving the hospital.

Six weeks after leaving the hospital, he walked 20 miles over a mountain road in one day, at an altitude of 6000 to 8000 feet, without undue fatigue or other ill effects. Thereafter, he resumed his usual practice of long, strenuous weekly walks. No studies on spermatogenesis were carried out. Twenty-eight months after exposure he remained well and able to work at a normal hard pace. No changes in his physical condition were noted on examination at this time.

All laboratory tests were within normal limits. These included kidney and liver-function tests; basal metabolism, electrocardiographic and hematologic studies. Slit-lamp examination of the cornea showed no evidence of scarring. Three years after exposure the patient was well and fit. Laboratory examination showed an initial granulocytosis. Although the level of lymphocytes was low (about 1000) there was no return to pre-exposure level in the 2-year period after exposure. A mild persistent eosinophilia began about 5 days after exposure. The decrease in platelet count to 300,000 from 400,000 noted after 24 days was temporary. The count was normal (500,000–600,000) by the 40th day. Sternal-marrow aspiration showed the marrow to be somewhat hypoplastic, particularly for myeloid cells and megakaryocytes. A small amount of radioactivity was measured in the sodium of the serum and urine and in the urinary phosphorus.

This case shows that exposure to a large dose of total body radiation can be sustained with no symptoms of injury. The only sign of body damage was the probable fall in the lymphocyte count. This is characteristic of, but not necessarily pathognomonic of, radiation injury, as the lymphoid tissue is one of the most radiosensitive of the body.

Summary

Abstracts of the case histories of three persons exposed to single doses of varying magnitudes of total body ionizing radiation (primarily neutrons and gamma rays) are presented. These cases serve to illustrate the lethal, sublethal and asymptomatic forms of the acute radiation syndrome. Although the exposures occurred as a result of inadvertent nuclear reactions (atomic explosions on a very small scale) the injuries were due solely to ionizing radiations. Flash burns and traumatic injuries due to heat and blast (such as were noted in 85 to 95 per cent of the Japanese victims of the atomic explosions) were not produced in these patients.

The author wishes to thank Dr. J. J. Morton, of Rochester, New York, for abstracting the case histories and for his advice in the preparation of this manuscript.

References

1. Hempelmann, L. H. Acute radiation injuries in man. *Surg., Gynec. & Obst.* **93**:385-403, 1951.
2. Hempelmann, L. H., Lisco, H., and Hoffman, J. G. Acute radiation syndrome: study of nine cases and review of problem. *Ann. Int. Med.* **36**:279-510, 1952.

LIBRARY MAR 27 1952 MANHATTAN

MEDICAL INTELLIGENCE

A HALF CENTURY OF GENERAL PRACTICE

DEAN S. LUCE, M.D.*

CANTON, MASSACHUSETTS

AT THE turn of the century the practice of medicine was in a state of flux. Surgery with the advent of antiseptics (1867) was advancing by leaps and bounds but was nevertheless endeavoring to extricate itself from the morass of methods of approach to operative fields and the vast number of different technics for the then common operations, trying to find the best solution to the various questions. Surgery has come a long way since Fitz (1886) published his article on appendicitis. In the early years of the century the preparation of the patient for operation and of the surgeon to render himself aseptic was formidable.

These were the horse-and-buggy days when the doctor carried his instruments and other needed articles in a little black bag. His pharmaceuticals were included among the articles, some in tablet form and some in the form of extracts and tinctures. Hospital practice existed in the large centers of population, although there was a trend toward the development of hospital facilities in buildings that had formerly been private homes. Patients had to be sold the idea of hospital care, and it was only by the doctor that the patient could be induced to become a hospital patient. Operations for conditions such as appendicitis and hernia were often performed in the homes on the kitchen table. Ether was almost exclusively used as an anesthetic.

Cupping was done, and occasionally phlebotomy — spinal puncture never. X-ray was just becoming useful as a diagnostic agent.

The progress of medicine as opposed to surgery was much slower in its development over the early part of the century, but with the growing enthusiasm and interest in organic chemistry and physics it has of late years made up for lost time.

The stethoscope was commonly used, but the old doctor with his ear to the patient's chest was often seen. No means existed for taking blood pressure. The Riva Rocci apparatus, one of the earliest forms of sphygmomanometers, was unsatisfactory for practical use.

To the young physician starting to do general practice in a community, obstetrics is the cornerstone of his medical life. Success in delivering a live baby to a new mother brings especial satisfaction to the doctor and makes a solid background for future employment in that family; right at this point his relation with it starts. If he supplements the delivery with successful pediatric care, he has sealed the bargain. The young doctor should remember that care of the baby through its growing years makes for future practice as he himself becomes older and his practice diminishes for natural reasons. As that baby grows to adult age, marries and has a family, his first choice on needing a doctor is his old family doctor, who has cared for him through the years.

During the late years of the first half of the century there has been an almost universal tendency for the prospective mother to have her baby in a hospital, but recently more has been said in favor of the advantages of home delivery to both the child and its parents. However, the consideration of expense has not yet been sufficiently stressed. The parents may legitimately look into this phase of the situation. Delivery at home is certainly much cheaper than deliveries in one of the large maternity hospitals, and with the now advocated few postpartum days' stay in bed, the mother if at home is in a position to superintend home affairs much earlier than she could have done had she had a hospital delivery. Of course, the doctor is helped greatly by having maternity cases in the hospital for delivery. He gives less time to a case and is less often rushed into premature operative delivery.

The fear of thrombophlebitis has brought about the condition of early ambulation. The patient is now told to get out of bed a day or two after delivery instead of remaining in bed from two to three weeks. The result of this treatment over a period of years is yet to be seen.

Cesarean section occupies a much more prominent place in the delivery of cases of difficult abnormal positions of the child in utero, due to perfection of technic and the use of antibiotics.

The utopian dream of obstetricians has yet to be realized — painless childbirth. We have run the gamut of methods of treatment from hypnotics to twilight sleep, even including thought control. At present we are interested in fearless deliveries.

After birth the baby passes into the field of pediatrics. The matter of feeding is of first importance. Here again we find that in half a century we have gone from breast to artificial feeding and now seem to be on our way back. The manufacturers of baby foods in many instances dictate to us how and what we shall feed our babies. This has been brought about through the years by the inability of the mother to nurse her baby, from lack of milk, sore nipples or abscess of the breast. The only alternative has been to feed the baby artificially. Fifty years ago it was thought that the newborn infant was not to go to the breast until the milk started, with the result that when that occurred the baby

*Dr. Dean S. Luce, of Canton, Massachusetts, was the American Medical Association General Practitioner of the Year in 1950.

had passed the time when he was eager to eat and now refused to nurse, with the resulting caked and sore breasts.

Before the present method of feeding was adopted, babies' food was made on a percentage basis, the problem being to make cow's milk resemble mother's milk in make-up. This was worked out by algebraic formula and resulted in a not altogether satisfactory solution. Diarrheas of several varieties — simple fermentative, iliocolitis and cholera morbus — often developed, and the baby had a hectic first two years of life. The family doctor was busy during the summers washing out bowels. With the pasteurization of clean milk these bowel disturbances were removed; their children's babyhood is now a pleasure to the parents.

After the second year of life the contagious diseases enter the picture. Of these, diphtheria was by far the worst, but thanks to immunization in the early months of life, diphtheria is now rarely seen. Should, however, a case be found, an adequate injection of antitoxin is the recognized proper treatment. The general practitioner may be able to perform a tracheotomy if necessary, but it is questionable that he has even heard of intubation, a procedure in which every medical student had to be proficient in the days before immunization.

Scarlet fever formerly required a quarantine of from six to eight weeks, or until all the peeling had disappeared. As the palms of the hands and soles of the feet were very slow in clearing, the quarantine period frequently extended beyond the six-week period. The patient was confined in bed in an isolated room with carbolized sheets covering the doorway.

Measles, with no abortion or modification by immune serum, involved treating the patient in a room totally dark, for eye protection.

Tuberculosis of the lungs evidenced by rales in the chest, significant of well developed disease, and bone tuberculosis were commonly seen in hospital clinics. Early diagnosis of this disease and adequate treatment have largely eliminated these advanced cases of tuberculosis.

Persistent headache of unknown origin occurring in the summer and early fall may be the guide leading to the ultimate diagnosis of typhoid fever. This disease was formerly prevalent at this time, over 50 per cent of the beds in a large hospital being taken for it. The morbidity and mortality were high. The sickness extended over weeks. This disease has about disappeared due to general sanitation, good sewage disposal and clean water supplies.

Pneumonia has been conquered by antibiotics. It has dropped from being the Number One cause of death almost to a condition requiring only office treatment. As a result of the study of pneumonia by pneumococcus typing (1931 to 1935) a system of treatment of the disease by serum was begun, but this was soon followed by the advent of the sulfa drugs and later by other antibiotics.

Malaria of the tertian type, formerly found in areas near Boston, is almost never seen, except in returning war veterans.

Diabetes is now successfully treated by diet and insulin, and the anemias are far better cared for with iron and liver than at the century's turn.

Medicine through the last fifty years has advanced by slow, tedious processes, often redoubling its steps and arriving again at the starting point. We now have a plethora of laboratory tests applicable to the diagnosis of many diseases; this has resulted in a tendency to rely on them to the exclusion of the old sound methods of diagnosis. These tests are the result of the present era of research, which through chemistry, physics and biology has led us into hitherto unknown fields. They are now in the process of evaluation and cataloguing. In this age of research has arisen the trend toward specialization, until the disease is often considered to the exclusion of the host. The art of the practice of medicine seems at times to be forgotten and the patient-physician relation relegated to the background. The practice of medicine consists of the prevention and care of disease and the alleviation of suffering. In considering this task it must never be lost sight of that the physician–patient relation is a personal one.

At the beginning of the century the family doctor, making his rounds by horse and buggy, had a radius of activity of perhaps six miles. The telephobe, then just coming into use, has enormously widened the doctor's field of activities. The patient now receives advice by telephone that previously he could only obtain at a personal visit. Physicians after World War I tended to settle in larger communities, which resulted in a shortage of doctors in the more rural areas, but by and large the family doctor could still be found in these larger centers of population, where his views on the practice of medicine were widened, due to his hospital affiliations. The patients, on the other hand, have moved to more urban areas, which makes the shortage of general practitioners seem more acute than is really the case.

The practice of medicine in this mid-century era is still in a state of flux. It is not static but is readjusting itself to the changing times. The family doctor should still be the first aid in time of sickness, and he should assume his place in the composite picture of modern medicine.

553 Washington Street

THE PERFECT MURDER

Perfection has always, and perhaps rightly, been considered suspect. Blemishes, like beauty spots, call attention to the virtue with which they are surrounded. Thus with our *Journal*, although errors and solecisms are not deliberately introduced to

break the monotony, their occasional occurrence is accepted with equanimity.

The following letters indicate minor lapses that can hardly be regarded as examples of studied carelessness, but not for worlds should they have been caught and corrected.

To the Editor: The medical progress report on "Diseases of the Thyroid Gland" by Cope that appeared in several recent issues of the *Journal* is masterly. Comprehensive yet concise, definite in statement but never dogmatic, calling attention to progress but indicating much yet to be done — these contributions are admirable.

One statement, however, filled me with amazement, horror and abomination. Cope discusses the possible carcinogenic effect of the use of radioactive iodine to relieve hyperthyroidism. Although he agrees that the possibility of late malignant degeneration after radioactive-iodine therapy is probably negligible, he admits that a long-term follow-up of a large series of cases will finally determine the safety or danger of this procedure.

Then on page 411 of the *Journal* of March 13 appears the statement that makes me shudder. "One patient was murdered eight years after such treatment and the thyroid gland was obtained at autopsy." This is indeed the ultimate in scientific zeal. Did the courts of Massachusetts hold that this was justifiable homicide?

LLEWELLYN SALE, M.D.

St. Louis, Missouri

Note: The word usually employed is "sacrificed." — ED.

To the Editor: At the conclusion of Case 38122 of the Case Records of the Massachusetts General Hospital (in the March 20 issue of the *Journal*), "A Physician" made a comment that reminded me of an old friend: "A man named Berry found aneurysms, called Berry aneurysms, of the middle cerebral artery in patients with polycystic kidneys." The fact of the matter, and I shall get away from the fact after this single statement, is that a physician named Collier, in studying aneurysms of the cerebral vessels, likened them to little berries, since which time some physicians have persisted in calling them berry aneurysms. It is the opinion of some others that this addition to the fruit-and-vegetable terminology of medicine should be torn down from the vine and buried.

My earlier acquaintance with Dr. Berry came while I was correcting examination papers two or three years ago. The diagnosis in the problem case was considered by several members of the class to be "rupture of an aneurysm of Berry." One student preferred to ignore Dr. Berry and Dr. Collier and advised me that the trouble was caused by a "secular aneurysm," the assumption probably being that spiritual or ecclesiastical aneurysms ought not to behave badly. But the paper that upset me most was that of a student who referred repeatedly to the offending anomaly as a "beriberi aneurysm."

I am sure that this is not the end of the subject. I look forward to the day when the anonymous and ever-present "A Physician" will describe "Saccula aneurysms, discussed by a physician named Saccula."

JOSEPH M. FOLEY, M.D.

Boston, Massachusetts

Let it be hoped that the accuracy for which we strive will never be achieved.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38201

PRESENTATION OF CASE

A twenty-four-year-old woman was admitted to the hospital because of abdominal swelling and fever.

Eleven months before entry, the patient had noted the gradual onset of swelling of the legs and abdomen. With this she developed mild exertional dyspnea and a fairly severe nonproductive cough. Four months before admission a diagnosis of acute rheumatic fever was entertained by her physician and she was given digitalis; this produced complete relief of the dyspnea, edema and ascites, which had been becoming progressively worse. However, one month later these symptoms recurred; four blood cultures taken at this time were negative. Six weeks prior to admission the abdominal swelling and the temperature rose to 101 to 102°F. and remained elevated until entry. She had no other symptoms until one week before admission, when a constant severe dull aching developed in the left upper quadrant.

There was no history of nosebleeds, joint pains or rheumatic fever. At twenty years of age she had experienced 4 or 5 five-minute attacks of sudden rapid beating of the heart, associated with faintness. Ten years before her admission a brother had died at the age of seventeen, after one year of congestive failure; he had been persistently hungry, had to eat between meals frequently and had had one low blood sugar while in the hospital. A postmortem examination had not been permitted.

Physical examination revealed a tall, slim girl in no distress. The neck veins were distended to the angle of the jaw but did not pulsate. There were rales and decreased breath sounds at the right base and dullness at the left base. The heart was enlarged to the anterior axillary line. The rhythm was regular except for runs of extrasystoles, and a diastolic gallop was heard best at the apex. A short Grade I systolic murmur was heard in the pulmonic area and in the third interspace to the left of the sternum. The pulmonic second sound was louder than the aortic; the mitral first sound was not accentuated. The abdomen was distended

with fluid and the liver was percussed 2 to 3 fingerbreadths below the right costal margin. There was slight pitting edema of the ankles.

The temperature was 98.6°F., the pulse 92 and the respirations 20. The blood pressure was 120 systolic, 60 diastolic.

A urinalysis was negative. Examination of the blood showed a hemoglobin of 11.2 gm. and a white-cell count of 10,100, with 74 per cent neutrophils. The sedimentation rate was 0.9 mm. per minute. The nonprotein nitrogen, total protein, albumin-globulin ratio and a fasting blood sugar were normal. The bromsulfalein retention was 12 per cent and the alkaline phosphatase was 6.6 units per 100 cc. The venous pressure was 250 mm. of saline, the circulation time (arm to tongue) 23 seconds and the vital capacity 1.1 liters, or 36 per cent of normal. An electrocardiogram showed an indefinite basic rhythm that was questionably either nodal or a normal sinus rhythm. There was occasional bigeminy and there were nonspecific T-wave changes. By phonocardiogram definite but faint decrescendo systolic and diastolic murmurs were made out in all areas, particularly in the pulmonic area. Roentgenogram of the chest demonstrated a moderate pleural effusion on the left and somewhat prominent pulmonary vessels. The heart was considerably enlarged, apparently in all chambers (Fig. 1).

Five thousand cc. of fluid was removed by abdominal paracentesis; it had a specific gravity of 1.018 and contained 4.1 gm. per 100 cc. of protein. Following this, the liver was palpable for a considerable distance below the costal margin. The patient was treated with digitalis, a moderately low salt diet, ammonium chloride and Mercuhydrin and was discharged on this regimen.

A week following discharge she was admitted to the House of the Good Samaritan for further treatment. On admission there, the neck veins were distended, there was a marked protodiastolic gallop, accentuated by inspiration, over the entire precordium and the remainder of the heart findings were as before. The abdomen was distended by fluid. The antistreptolysin titer was less than 50. Electrocardiogram revealed a tendency to low voltage, with low inversion of T waves in Leads 1, 2 and 3 and in the six precordial leads. There were frequent ventricular premature beats. No P waves were visible, but esophageal leads showed the dominant rhythm to be auricular flutter with a 2:1A-V block, with an auricular rate of 220 and with a ventricular rate of 110. Electrocardiograms taken two hours after 0.5 gm. of Pronestyl revealed no ventricular premature beats. A venous glucose-tolerance test showed the following: fasting 61 mg.; one hour 92 mg.; 2 hours 96 mg.; 3 hours 75 mg.; four hours 53 mg. per 100 cc. (with hypoglycemia symptoms). A repeated oral and an intravenous glucose-tolerance test were all within the normal range. An epinephrine test using 0.5 cc. of 1:1000 solution showed all specimens to be over 140 mg. per 100 cc. and an eosinophil count dropped from 725 to 250 cells per cu. mm. A Congo red test showed 71 per cent retention in the serum. For the first seven weeks the patient was on bed rest, low-sodium diet, digitalis, Mercuhydrin and Pronestyl. On this program her weight remained constant and ascites and lower-abdominal pain continued. She then received ACTH, 40 mg. per day for four weeks. After four days of hormone therapy, plus daily mercurial diuretics, she developed a massive right pleural effusion that had to be relieved by thoracentesis;

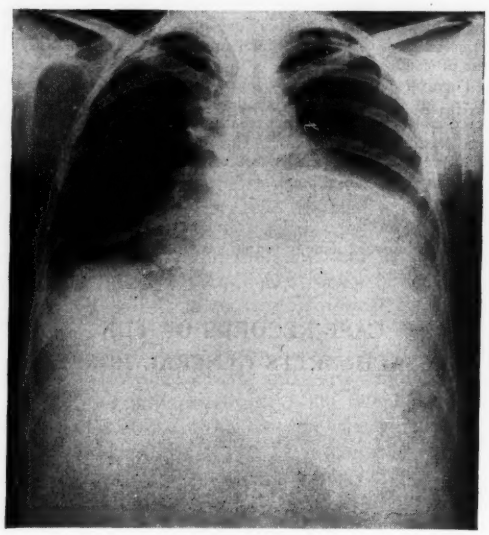

FIGURE 1.

during the period of accumulation of pleural fluid the ascites decreased. Following the thoracentesis the pleural effusion rapidly reaccumulated sufficiently to cause a mediastinal shift. Therapy was continued, however, and the amount of fluid in the right chest and the ascites decreased spontaneously. Following this the liver edge could be palpated 7 cm. below the costal margin. After omission of the ACTH, there was a prompt diuresis with a nine-pound weight loss in five days; the pleural effusion and ascites were no longer detectable. The venous pressure during ACTH therapy was equivalent to 270 mm. of saline and after treatment dropped to 160 mm. Six days after cessation of therapy an x-ray film of the chest revealed a slight decrease in the heart size. The patient was discharged from the House of the Good Samaritan after three months.

For the remainder of her life, — fourteen months, — the patient lived at home and was seen fre-

quently in the Cardiac Clinic. During this period she was treated with quinidine, digitalis, a low-sodium diet, Theocalcin, Pronestyl, mercurial diuretics and restricted activity. A roentgenogram five months after discharge showed that the heart shadow had decreased in size (Fig. 2). Gradually the signs of congestive failure, which had been minimal at the time of discharge from the House of the Good Samaritan, began to increase. Over the last several months of her life she noted dull crampy right upper-quadrant and epigastric pain. During the last six months she had 1 to 2 attacks per week of sudden palpitations with nausea, precordial pain and dizziness. A roentgenogram three months before death showed pleural effusion on the right and again considerable enlargement of the heart shadow (Fig. 3). She died rather abruptly at home. A relative stated that she had run out of some of her medications a week previously.

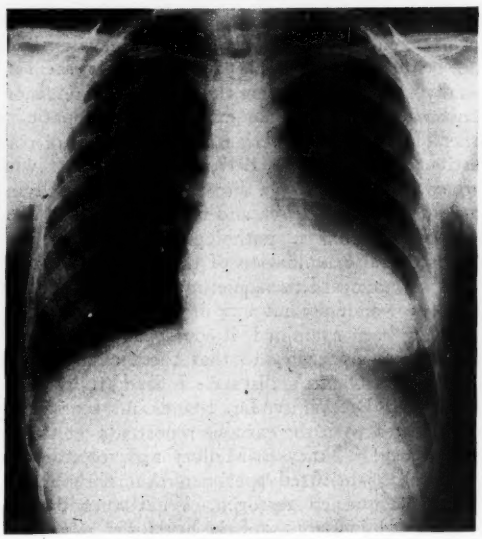

FIGURE 2.

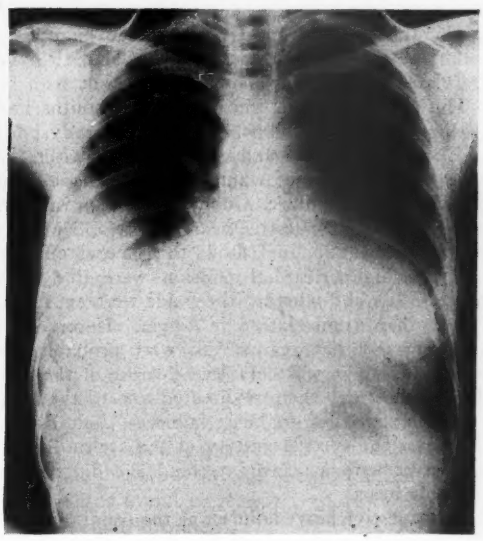

FIGURE 3.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE*: May I see the electrocardiograms? . . . In the first group of electrocardiograms taken at the time of admission, it is difficult to see any auricular activity. The normal ventricular complex is very small, and there are premature beats. Then by the time the second one was taken, there were no premature beats but tachycardia.

DR. BENJAMIN CASTLEMAN: The second set of electrocardiograms was made three days later.

DR. SPRAGUE: In the last ones, made about ten months after discharge, there is a very low ventricular complex and nonspecific T-wave changes probably influenced by the digitalis.

DR. PAUL D. WHITE: Can you make out the flutter?

DR. SPRAGUE: That was evident only in the esophageal leads, which I believe we do not have here.

DR. ALAN FRIEDLICH: I think the esophageal leads were taken at the House of the Good Samaritan.

DR. SPRAGUE: May I see the x-ray films.

DR. STANLEY M. WYMAN: The original examination, made about a year and a half before death, shows great enlargement of the abdomen at the time she had the ascites, and there is fluid in the left pleural space, which is best visualized in the lateral projection lying posteriorly. The heart shadow is very large, and its lower right border has a rather acute angle (Fig. 1). There is no specific chamber enlargement that I can detect; particularly, the left auricle does not seem very large as seen in the lateral view. I do not know whether the patient was fluoroscoped at this time, although I assume she was. There is no note in the record about the quality of pulsations of the heart shadows.

DR. CASTLEMAN: Can you answer that, Dr. Friedlich?

DR. FRIEDLICH: Pulsations were seen, but they were of diminished amplitude.

DR. WYMAN: The next examination, made about five months later, shows a great change. The

*Associate physician, Massachusetts General Hospital.

ascites in the abdomen has disappeared, the fluid in the pleural cavity has disappeared and the heart shadow, or what we take to be the heart shadow, is very much smaller (Fig. 2). Again, I can make no definite statement about specific chamber enlargement, although I think the right ventricle may be considerably enlarged. The last films show the massive right pleural effusion. The heart is displaced to the left but probably has not changed much otherwise (Fig. 3). I do not see much pulmonary vascular congestion at that time.

DR. WHITE: The heart looks bigger in the last examination.

DR. WYMAN: I do not know how much of the shadow is the heart itself and how much is fluid in the medial aspect of the left pleural space.

DR. WHITE: The left border of the apex looks more rounded.

DR. SPRAGUE: I do not know the diagnosis in this case, and I do not know what other tests I would like to have, short of a cardiac biopsy, to make the diagnosis. I shall be very glad to have Dr. Castleman tell me what this is all about.

This young woman, who for eleven months had swelling of the legs, ascites, a variable fever, dyspnea and cough, died two and one-half years after the onset of symptoms of what appears to have been congestive heart failure. One may question whether or not this was congestive heart failure and wonder whether the abdominal fluid, the pleural effusion and possible pericardial effusion were due to a polyserositis and whether the fluids were exudative rather than transudative in origin. However, it seems to me that against this were probably the following: There was complete clearing of the condition twice with therapy directed toward the management of congestive heart failure — digitalis and diuretics; the specific gravity of the ascitic fluid is consistent with a transudate; and she did have a very big heart.

If congestive heart failure was the condition here, what was the etiology? I suffer from an embarrassment of riches as far as the etiology is concerned in this situation. Rheumatic heart disease was suspected, but there was no history of joint pains or nosebleed, no valvular involvement, a low antistreptolysin titer and a very bizarre course. It is true that a phonocardiogram demonstrated faint murmurs in both systole and diastole, which I find difficult to utilize in the diagnosis, except as functional murmurs. I do not believe I can bring in cor pulmonale here in the absence of cyanosis or right-axis deviation in the electrocardiogram.

I might consider next whether there are any types of congenital heart disease that could give this picture. I would have to stretch my imagination a great deal to invoke congenital heart disease, but one might think of the possibility of endocardial fibrosis, such as may occur in more than one child in a family. However, I do not know that it ever occurs as late in life as this, at least in this country. The so-called "idiopathic hypertrophy," which is a catch-all that has become smaller as the years have gone on and we have been able to pull out of it more definite etiologies, is a questionable diagnosis, even in childhood.

Then I come to the condition the physicians apparently were thinking of here — von Gierke's disease or glycogen-storage disease, an obscure myocardial process that every so often comes up as a possibility in adult life. Various tests for glycogen-storage disease were made. The fasting blood sugar is low in this disease, sensitivity to insulin is increased, elevation of blood sugar after injection of epinephrin is reduced to less than 35 mg. per 100 cc. in 40 to 60 minutes and there may be ketonuria without glycosuria. In the cardiac type, however, enlargement of liver and kidneys is slight and fasting hypoglycemia and ketonuria are said usually to be absent. Here these tests were not more abnormal than could be explained by hepatic or other glandular dysfunction in the presence of congestive failure. Up to 1947, only 2 patients with proved glycogen-storage disease of the heart, living to the top ages of eleven and fifteen years, had been described. From a pathological standpoint the microscopical examination of the muscle in bizarre types of myocarditis sometimes shows vacuoles; then one wonders what was in the vacuoles and if, had they been examined, it could have been shown that it was glycogen and that these changes were due to von Gierke's disease. Indeed, it was that pitfall that Dr. White, Dr. Bland and I originally encountered with the case we reported over twenty years ago[1]; Dr. Tracy B. Mallory was able to prove later on in the fixed specimen that the vacuoles actually contained glycogen. What we had called idiopathic hypertrophy of the heart was an example of von Gierke's disease. I like the name "thesaurismosis glycogenica," which means that some organs of the body are treasuries or depositories of glycogen. Another point is that this patient's brother died at the age of seventeen with an indication of some difficulty with the carbohydrate mechanism — hunger and hypoglycemia. Did he have some hyperinsulinism, or could it be that he had the same disease — that it was familial and that in some way it could persist until the age of twenty-four? In the cases that we reported there was a rather striking familial incidence of heart disease in children in direct or collateral lines.

Among the collagen diseases, I have ruled out rheumatic fever to my own satisfaction. I do not see any reason for making a diagnosis of disseminated lupus erythematosus; there was no skin rash and no joint pains. Polyarteritis nodosa might be a possibility, although that is commoner in later life and in men in the forty- to fifty-year range. There was abdominal pain in this case, which may be a feature of this disease. It appears that cardiac

failure in polyarteritis is late, but I note that in 6 of Griffith's 17 recently reported cases[2] the terminal event was congestive heart failure. Here there was no eosinophilia or nodules, but in this disease you do not have to wait until you have all the classical signs to suspect the diagnosis.

Another condition to consider in this case is amyloidosis. There was no origin for secondary amyloidosis. The Congo red test was negative but probably would not be diagnostic if amyloid deposits were small. At present there are not enough data relative to the Congo red test in primary amyloidosis of the heart to make it certain that the test is specific.

There seems little likelihood that we are dealing with tumor; there was not the relentless downhill course of malignant disease, as the patient did improve twice. I think I may rule that out.

Pericardial disease must of course be considered in a young person who has ascites as a predominant sign. It seems likely to me that at least there had been some fluid in the pericardium, but I think all the fluid could have been a transudate instead of an exudate of inflammatory origin. This patient's course was not that of constrictive pericarditis. The heart, — at least the ventricle, according to the protocol, — did not decrease much in size when the fluid in the chest disappeared; the heart was big, whether or not there was fluid in the pericardium.

I come to the matter of a diffuse unexplained myocarditis, which comes up fairly frequently in these sessions. Gore and Saphir,[3] in their army report, listed about 50 different causes of myocarditis, ranging from the unexpected acute myocarditis following mild respiratory infection to such types as the well known diphtheritic and rheumatic myocarditis and also a group of unexplained etiology. I do not see any point in cataloguing these, because there was nothing specific in this case to direct us to draw any one of them out of the grab bag. There has been some interest recently in a granulomatous myocarditis, question of sarcoidosis, but specific cardiac sarcoidosis has been found only in the Negro, with, I think, only one exception, a white male. We have here the possibility, it seems to me, of some type of interstitial myocarditis or possibly interstitial edema, often unexplained. Perhaps there were vacuoles in this myocardium; perhaps there were mural thrombi with embolism, which is quite common in this condition. The enlarged heart, the gallop rhythm, the ectopic rhythm and the T-wave change would all go with that. It is true that there was not the intraventricular block that I would like to see for a surer diagnosis of myocarditis. I do know of persons with this "idiopathic myocarditis" who lived as long as four years.

ACTH was probably used empirically. I do not want to cast any doubts on the therapeutic acumen of our associates at the Good Samaritan, but I think that "when in doubt use ACTH" was the presumption here. Cortisone has had a beneficial effect on nonspecific myocarditis, at least temporarily. I think it was well stated recently that "the steroid hormones have the ability to mask all signs except those of death."

I am left with a probable diagnosis of myocarditis of unknown etiology with a terminal ectopic rhythm, perhaps ventricular tachycardia, and possible pulmonary embolism. There may have been some other obscure endocrine situation here. I am very unsure of my diagnosis, but, in hunting terms, if I did not kill the fox at least I have had a very good run.

Dr. White: This patient was sent to the House of the Good Samaritan for the chief purpose of receiving ACTH therapy under prolonged observation. She was shown at Medical Grand Rounds[4] and also at rounds in the Good Samaritan as a problem case, with particular reference to the familial occurrence of disease like this. A brother had died; were there any other siblings who had this condition?

Dr. Friedlich: She had five sisters; all were examined and were found to be normal.

Dr. White: Our previous experience with siblings who had heart disease of unknown origin had been that they were of the same sex — 3 or 4 pairs of brothers and 1 pair of sisters. We wondered if we might have here an exception to our previous experience, that a sister and brother had the same strange condition. We were puzzled and went through much the same reasoning as Dr. Sprague has done. I might add that in the case of 2 pairs of siblings, 1 of a pair of brothers and 1 of a pair of sisters underwent surgery because of the possibility of constrictive pericarditis, which was not found. The diagnosis had not been made clinically, but we wanted to rule pericarditis out, since it might have been cured if present.

Clinical Diagnosis

?Idiopathic familial cardiac hypertrophy.
Congestive failure.

Dr. Sprague's Diagnoses

Myocarditis, etiology unknown.
Ectopic ventricular tachycardia.
?Pulmonary embolism.

Anatomical Diagnoses

Cardiac dilatation of right heart, extreme, ?congenital.
Mural thrombi, right auricle and ventricle.
Hydrothorax, bilateral.
Cardiac cirrhosis.
Old infarcts of kidneys.

Pathological Discussion

Dr. Benjamin Castleman: The heart in this case (Fig. 4), although it was markedly enlarged, did not weigh much — just under 300 gm.; the enlargement was due to extreme dilatation of the right side of the heart. The right ventricle and auricle were huge and very thin — the thinnest that I have ever seen. In places the ventricle was not over 1 mm. in thickness.

Dr. White: Do you think the wall was pliable enough to give this acute angle, which is ordinarily encountered with pericardial fluid?

Dr. Castleman: Probably. I have never seen a paper-thin right ventricle like this before. The left

Figure 4. *Opened Ventricles, Showing the Hugely Dilated Right Ventricle and the Normal-Appearing Left Ventricle.*

ventricle was normal. I do not understand why there should not have been right-axis deviation.

Dr. White: Perhaps there was not enough muscle.

Dr. Castleman: Dr. David Kahn measured the thickness of the muscle fibers and found that those of the left ventricle were normal in size — between 15 and 20 microns. Those on the right were bigger — between 20 and 25. There was a great deal of edema between the individual muscle fibers, so that the bundle was big and the fibers were separated from each other. There was no evidence of sarcoidosis, glycogen, amyloid or inflammatory reaction.

Dr. White: No fibrosis?

Dr. Castleman: Very little fibrosis around the blood vessels. We estimated the volume of the right ventricle to be five times that of the left. In both right chambers there were a few mural thrombi such as one often sees in this group of cases that we know so little about, called idiopathic cardiac hypertrophy. The valves were normal and the coronary arteries were thin and widely patent.

Dr. White: Had any of the thrombi gone into the lung?

Dr. Castleman: No. In the left ventricle, there was slight endocardial fibrosis under the aortic valve such as we occasionally see in this group of patients.

Dr. White: None on the right?

Dr. Castleman: No; none that we could find.

Dr. Brailey: Were there any peripheral emboli?

Dr. Castleman: There were some in the kidney, old ones, but nothing recent. Each pleural cavity contained a liter and a half of fluid, but there was none in the abdomen. There was a mild cardiac cirrhosis of the liver.

Dr. White: The pulmonary blood pressure was never measured? I suppose in the future we should see if there is any pulmonary hypertension in these obscure cases. Was there any evidence of pulmonary vascular disease?

Dr. Castleman: No; there was nothing abnormal in the pulmonary vessels or in the other structures of the lungs.

Dr. White: Have you as yet had a chance to comb the literature for other similar cases?

Dr. Sprague: The only one I ever saw like this was the one that Harold Segall of Montreal demonstrated a few years ago from the Osler collection; that was paper thin all over and was called a "parchment heart."[5]

Dr. Castleman: Unlike the Osler heart, in which both right and left chambers were paper thin, in this heart the left was normal in size and thickness and on microscopical examination. I think the best bet is that it was congenital in origin.

Dr. Sprague: The present belief about endocardial fibrosis that occurs in infancy and childhood is that it is due to a persistence of the fetal architecture of the ventricle. I wonder if that could be possible on one side of the heart and not on the other.

Dr. Castleman: There was no evidence to suggest a myocarditis in fetal life or afterwards; there was not a single inflammatory cell anywhere.

A Physician: Was the septum normal?

Dr. Castleman: Yes.

Dr. Sprague: What are you going to call it, ectasia of the right ventricle?

Dr. Castleman: The right auricle was also ectatic.

References

1. Sprague, H. B., Bland, E. F., and White, P. D. Congenital idiopathic hypertrophy of heart: case with unusual family history. *Am. J. Dis. Child.* **41**:877-886, 1931.
2. Griffith, G. C., and Vural, I. L. Polyarteritis nodosa: correlation of clinical and postmortem findings in seventeen cases. *Circulation* **3**:481-491, 1951.
3. Gore, G., and Saphir, O. Myocarditis: classification of 1402 cases. *Am. Heart J.* **34**:827-830, 1947.
4. Cases from the Medical Grand Rounds of the Massachusetts General Hospital (Case 187). *Am. Pract.* **2**:890-894, 1951.
5. Segall, H. N. Parchment heart (Osler). *Am. Heart J.* **40**:948-950, 1950.

LIBRARY MAR 27 1952 MANHATTAN KANSAS

CASE 38202

Presentation of Case

First admission. A fifty-eight-year-old man entered the hospital because of weakness and tarry stools.

About four weeks prior to admission the patient first noted weakness and tiredness, which gradually progressed. Two weeks prior to entry he had an episode of epistaxis. For the week before admission he noted a headache each morning on arising, which was relieved by a bowel movement; the stools were normal in color and consistency. Two days prior to entry he became so weak that he was unable to work; his physician found the hemoglobin to be 5 gm. Except for a loss of appetite and some increase in gas, there had been no gastrointestinal symptoms. He had not noted any alteration in the color of his stools, and there had been no change in the frequency of bowel movements.

He had had a simple mastectomy for a "benign tumor" of the left breast thirty years before admission. For the five or six years before admission he had had nocturia (1 to 2 times) and for the two years prior to entry some hesitancy and weakness of the urinary stream. A cardiac abnormality was noted at one time on a routine chest roentgenogram, but he was studied at another hospital and told that he had no serious disease.

Physical examination revealed a well developed, well nourished, pale man. There was a scar on the left breast but no masses or lumps. The lungs were clear. There was a Grade II basal systolic murmur; the point of maximum impulse was at the anterior axillary line. The abdomen was normal. The prostate was non-nodular, nontender and diffusely enlarged to three times normal size.

The temperature was 99.5°F., the pulse 88 and the respirations 16. The blood pressure was 148 systolic, 68 diastolic.

A urine, of specific gravity of 1.008, gave a + reaction for albumin. Examination of the blood showed a hemoglobin of 5 gm. and a white-cell count of 10,850; the bleeding time and clotting time were normal. The nonprotein nitrogen was 33 mg. and the total protein 5.4 gm. per 100 cc. The prothrombin time was 16 seconds (normal, 14 seconds). A bromsulfalein test was normal. The stool was black and gave a ++++ guaiac reaction. A proctoscopic examination revealed no abnormality except for grossly bloody stool. Gastrointestinal series showed a hiatus hernia, rather prominent mucosal folds throughout the fundus of the stomach, some thickening of the mucosa of the duodenum and no evidence of varices. Intravenous pyelogram showed a huge intravesical prostate and normal-appearing kidneys. The roentgenogram showed an enlarged heart without characteristic configuration, moderate pulmonary congestion and a questionable enlargement of the spleen. An electrocardiogram showed nonspecific ST-segment and T-wave changes of no specific diagnostic pattern.

The patient was given eight blood transfusions and the hemoglobin increased to 14 gm. By the third day the bleeding appeared to have stopped. On this day the patient developed an acute urinary retention and the temperature rose to 104°F. An indwelling catheter was inserted; the urine contained many pus cells and red cells and on culture grew abundant *Bacillus coli.* After a week's treatment with aureomycin, streptomycin and penicillin, the temperature returned to normal and the urine cleared. One week later, he developed left-sided chest pain, coughed up a small amount of bloody sputum and had a temperature of 102°F. A chest x-ray film was suggestive of pulmonary infarction of the left lower lobe. A week after this episode, bilateral femoral-vein ligation was performed; at operation no evidence of thrombosis or phlebitis was found. A repeat gastrointestinal series showed the duodenal cap to be filled to a grossly normal contour, but on several films there was a suspicion of a small puddling of barium in the cap; the spleen appeared to be enlarged and the esophagus and stomach appeared normal. The patient was discharged after one month of hospitalization on catheter drainage, ulcer diet and orally given iron; he was afebrile, the stools gave a negative guaiac reaction and the hemoglobin was 11 gm. per 100 cc. He was to return in two weeks for further management.

Second admission (two weeks later). Shortly after discharge he noted that his stools became black and remained so throughout the interval. The stools had been well formed and there had been no diarrhea. He had had no weakness, faintness, dizziness, epigastric pain or discomfort.

Physical examination was essentially unchanged from his previous admission.

Examination of the blood revealed a hemoglobin of 9.7 gm. and a white-cell count of 8600. The prothrombin time was 16 seconds (normal, 14 seconds) and the bleeding time six minutes. The nonprotein nitrogen was 28 mg., the total protein 6.3 gm., with an albumin-globulin ratio of 1.4, and the alkaline phosphatase 2.8 units per 100 cc. The cephalin flocculation was negative in 24 and 48 hours, and the bilirubin was normal. A urine of specific gravity 1.020 gave a + reaction for albumin; the sediment contained 35 white cells and a rare granular cast per high-power field. The stools gave a ++++ guaiac reaction. A gastrointestinal series showed a small hiatus hernia and an enlarged spleen; no abnormality could be made out in the esophagus, stomach, duodenum or jejunum. A roentgenogram of the chest showed an area of density in the left lower lobe. A barium-enema examination was negative. A small-bowel barium examination demonstrated no obstruction, delay, filling defect or mucosal abnormality in the small intestine. In the right

lower quadrant a thin column of barium was demonstrated to lie outside the small bowel; on later films this was seen to be a barium-filled appendix. Esophagoscopy and gastroscopy showed no abnormality except for slight atrophy of the gastric mucosa.

The patient was kept on catheter drainage, placed on an ulcer diet and given a number of blood transfusions. On the sixth hospital day the hemoglobin was 12.4 gm. and on the eighth day 12.8 gm. The stools had become guaiac negative. On the tenth day an operation was performed.

Differential Diagnosis

Dr. Gordon A. Donaldson*: This is a very stimulating case; it brings up the old problem of where bleeding from the gastrointestinal tract takes place in the presence of repeated essentially negative x-ray examinations. I am going to have to make two or three premises and accept a few statements of fact that have been blown up rather prominently in the protocol. One is the fact that the patient had a breast tumor thirty years before admission, which must have been a benign tumor; otherwise I would not expect a male with a malignant breast tumor to be alive today. Secondly, the prostatic hypertrophy was probably also a benign process that produced changes in the urine and accounted for some loss of blood by urine and secondary changes in the kidneys. I doubt that the anemia could be accounted for on the basis of any amount of blood loss in the urine or that the persistent melena could have been due to the pelvic congestion caused by this large prostate. Evidently there was striking enlargement of the prostate, and I believe this can occasionally produce occult blood in the stool, if not gross blood, but I hesitate to accept that as a source. Finally, I am accepting as a blanket statement the fact that he had a pulmonary infarction that prolonged his initial hospital stay. It is worthy of comment that he had this thrombosis and infarction in spite of an episode of epistaxis and of bleeding from the gastrointestinal tract.

Having more or less settled these points, I think not too arbitrarily, I shall focus my attention on the following three facts: The patient had a cardiac abnormality with probable congestion, possibly responsible for the infarctions in the lung and the enlarged spleen. He had a splenomegaly that was repeatedly demonstrated by x-ray examination but was never picked up on physical examination. We have to remember, however, that he was a patient on the surgical ward, not on the medical ward. Finally, this patient had an anemia and melena in the face of negative gastrointestinal x-ray examinations. This brings me to the x-ray films, Dr. Hanelin. I should like to see just how big this spleen was.

Dr. Joseph Hanelin: One of the series of pyelogram films shows normal kidneys, a liver that is not enlarged and a spleen that is definitely increased in size, perhaps twice or better. The prostate is enlarged. Multiple gastrointestinal series were carried out, and in only one is there anything that might be regarded as suspicious of duodenal ulceration. This finding remains rather questionable as indicating a likely source of hemorrhage. The series of chest films running through the first and second admissions shows initially fairly normal-appearing lung fields except for some streaking at the left base. Subsequently he developed linear densities in the lower lobes of both lungs but more marked on the left side. In the films taken during the second admission, there is persistence of an abnormal process in the left lower lobe and changes on the left side entirely compatible with infarction.

Dr. Donaldson: Is the duodenum deformed?

Dr. Hanelin: No; it is not consistently deformed. It changes shape and appears freely distensible. It is only by virtue of the small barium fleck near the apex of the duodenal bulb that the possibility of ulcer was considered.

Dr. Benjamin Castleman: Could that lesion in the lung be a form of plate-like atelectasis?

Dr. Hanelin: Yes, I think it could, but in addition there is a larger lesion in the left lower lobe that I think is compatible with infarction.

Dr. Donaldson: How big was the hiatus hernia?

Dr. Hanelin: The hiatus hernia was quite small. It is not shown in these films. The barium-enema examination is negative. The streak of barium referred to is in the appendix. The small-bowel examination shows a grossly normal intestinal tract.

Dr. Donaldson: I would like to begin the discussion by considering the intestinal tract; I suppose I ought to start with the lower gastrointestinal tract. Diverticula of the colon are occasionally responsible for this type of melena, but there was no evidence of any here. Tumor has been ruled out by Dr. Hanelin. Meckel's diverticulum should obstruct rather than bleed in a patient of this age. There is one disturbing finding in the examination of the lower intestinal tract; that is that grossly bloody material was seen on proctoscopic examination. On the other hand, this may be found occasionally in patients who have upper-intestinal bleeding. It is possible to put blood in the stomach by Levine tube, — 200 to 300 cc., — and find on proctoscopic examination an hour or two later cherry-red blood coming down through the sigmoid. I suppose this is dependent on the rate of intestinal activity. I do not wish, therefore, to place the disease in the lower bowel on the basis of this finding alone.

To go to the upper intestinal tract, I think gross tumors of the stomach are ruled out by x-ray examination. I cannot exclude a small leiomyoma, hemangioma or neurofibroma, which are reported by pathologists to be present in the stomach and duodenum in a fairly high percentage of cases. This is particularly so of leiomyomas of small size

*Assistant surgeon, Massachusetts General Hospital.

but of a size insufficient to cause this amount of bleeding. There were no diverticula in the upper gastrointestinal tract. Duodenal ulcers, ulcers not evident in the x-ray films, occasionally account for this type of bleeding. They are perhaps a more frequent source than gastric ulcers, although gastric ulcers are more difficult to visualize by x-ray examination because of the size and contour of the stomach. These small erosions can exist particularly in the antral portion of the stomach, and no number of x-ray films will demonstrate them. I think that erosions rather than ulcers in the stomach are a very definite possibility. Esophageal varices are ruled out by Dr. Hanelin, and the negative liver tests support the x-ray report. Diaphragmatic hernia as a possible source of slow oozing is worth considering. The small hernias are more likely to cause this type of bleeding than the large ones, as they become constricted and congested, resulting in an oozing type of bleeding. The gastroscopist found an atrophic gastritis, which may be associated with superficial ulceration or erosions.

Finally, among the causes of occult gastrointestinal bleeding should be mentioned aneurysm of one of the gastric arteries. This is a rare finding, but there have been 3 cases in this hospital[1] over the past three years, and the rate of bleeding may be of this nature. It is more often gross enough to cause shock, and there may be repeated hemorrhages, relieved only by surgery.

At the bottom of the wastebasket is the possibility of a blood dyscrasia. The bleeding time, clotting time and prothrombin time were normal. Is there a report of a smear in the record, Dr. Castleman? I think a smear should have been done — more than once.

Dr. Castleman: The only smear showed normal platelets and no reticulocytes.

Dr. Donaldson: Along with this normal laboratory work and the thrombosis with embolism is the history of epistaxis, melena and a large spleen. What bothers me through the whole record is the fact that in spite of negative guaiac tests the hemoglobin dropped on two occasions, once as much as 3 gm. I wonder whether there may have been a primary splenic disease and the operation performed was a splenectomy. I doubt this, however, and believe that a blood dyscrasia is unlikely.

The splenomegaly, such as it was, is not very striking. Dr. Jacobson has recently informed me that an enlarged spleen discovered only on the x-ray film is not too significant and that it becomes important only when it is palpable. Could this enlargement have been secondary to chronic blood loss and perhaps compensatory enlargement of the spleen? Here again, I am told that spleens do not enlarge in the presence of chronic blood loss unless there is also some iron-deficiency anemia. To explain this splenic enlargement, I then have to think of an infection and tie this up with the gastrointestinal bleeding. It seems very unlikely. Lymphoma also comes to mind. The likelihood of lymphoma in the stomach wall unobserved by x-ray examination is very definite; however, a lymphoma that has bled this much must be an ulcerating one, and there was no evidence of ulceration on the x-ray films. Cirrhosis is more or less ruled out by negative liver findings. Banti's disease or congestive splenomegaly with gastric bleeding due to congestion is also a far cry, as the spleen was not big enough for a Banti spleen.

This patient had a mild degree of congestive heart disease, as demonstrated by the x-ray films and the examination of the lungs and spleen. Could he have bled into his gastrointestinal tract from a process that was perhaps aggravated by cardiac congestion? The primary source is anybody's guess; I think he was operated on with the idea of finding out where the bleeding originated, and as a long shot I shall say it was due to erosion of the mucosa in the gastric antrum or in the duodenum or possibly to a gastric-artery aneurysm.

Dr. F. Dennette Adams: I would hesitate to accept Dr. Donaldson's explanation of the splenic enlargement. Ordinarily, one does not find the spleen enlarged because of mild or moderate congestive heart failure. Decidedly against so-called Banti's syndrome or portal hypertension as a cause of the bleeding is the elevated white-cell count; leukopenia is the rule with the disturbances in this group. However, I have no explanation to offer. I think he bled from a duodenal ulcer.

Dr. Bernard M. Jacobson: Has Dr. Hanelin absolved the small bowel?

Dr. Hanelin: I saw no evidence of trouble in the small bowel.

A Physician: What was the nationality of the patient?

Dr. Castleman: He was born in Italy.

A Physician: I think we see really large spleens in many persons born in Italy.

Dr. Jacobson: I think that is a good point. About 5 to 10 per cent of our local population of Mediterranean origin have a mild degree of Mediterranean anemia; this spleen may have been due to asymptomatic Mediterranean anemia and may not have had any bearing on the present illness.

Clinical Diagnoses

Gastrointestinal bleeding.
Hypertrophy of the prostate.

Dr. Donaldson's Diagnosis

?Erosion of the gastric or duodenal mucosa.
?Aneurysm of gastric artery.

Anatomical Diagnosis

Leiomyosarcoma, low grade, of ileum.

Pathological Discussion

Dr. Castleman: This patient was operated on because the surgeons could not demonstrate the cause of the bleeding from the intestinal tract. At operation, a mass was found in the ileum about 4 feet from the ileocecal valve that had produced a dimple of the serosa. This section of ileum was removed, and a round polypoid tumor was found projecting into the lumen; on its mucosal surface was a definite small ulceration (Fig. 1), undoubtedly the source of the trouble. The tumor measured under 2 cm. in diameter and microscopically was a spindle-cell tumor that we called a leiomyosarcoma of low-grade malignancy.

Dr. Donaldson: Is that the entire specimen?

Dr. Castleman: Yes; the surgeons found the lesion very easily after they opened the abdomen, because they were able to feel it; they merely performed a small resection.

Although many leiomyomas of the stomach are found incidentally by pathologists, we have often seen bleeding from them; I remember one that was about 1 cm. in diameter that bled off and on for over ten years.

Dr. Donaldson: I tried to find the reference to an article discussed at the New England Surgical Society meeting last year in which a very high incidence of small leiomyomas in the stomach and duodenum was reported.

Dr. Castleman: That depends on how carefully the pathologist wants to examine the stomach for these tumors. In the Palmer Memorial and Deaconess hospitals Meissner[2] made a careful study of the

Figure 1.

stomach from 50 routine autopsies and found an incidence of 46 per cent of symptomless small spindle-cell tumors; most of them were leiomyomas. Some of them may have been neurofibromas, but it is an academic point, as they both produce the same type of symptoms when they ulcerate.

References

1. Donaldson, G. A., and Hamlin, E., Jr. Massive hematemesis resulting from rupture of gastric-artery aneurysm. *New Eng. J. Med.* **243**: 369-373, 1950.
2. Meissner, W. A. Leiomyoma of stomach. *Arch. Path.* **38**:207-209, 1944.

Massachusetts Physicians Art Association

5. *Wintertime in New England*

(*Exhibited at Atlantic City, 1947*)

Oil Painting by

Charles A. Lamb, M.D.

Assistant Professor of Surgery

Tufts College Medical School

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society
Owned by the Massachusetts Medical Society and Published Weekly under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. Richard E. Alt, M.D.

Joseph Garland, M.D., Editor

Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Theodore H. Ingalls, M.D.

Clara D. Davies, Executive Editor
Robert O'Leary, Assistant Editor*
James F. Ballard, Book Review Editor

Editorial Board
C. Guy Lane, M.D. C. Stuart Welch, M.D.
Henry R. Viets, M.D. Vernon P. Williams, M.D.
Robert M. Green, M.D. Benjamin Castleman, M.D.
Dwight O'Hara, M.D. Hugh R. Leavell, M.D.
Fletcher H. Colby, M.D. J. Englebert Dunphy, M.D.
Robert L. Goodale, M.D. Robert W. Buck, M.D.
Chester M. Jones, M.D. Herrman L. Blumgart, M.D.
Harvey R. Morrison, M.D. Frank N. Allan, M.D.
Maxwell Finland, M.D. Harvey A. Kelly, M.D.
Deering G. Smith, M.D.†

*On leave of absence with the Armed Forces.
†Representing the New Hampshire Medical Society.

Subscription Terms: $8.00 per year in advance, postage paid, for the United States (medical students and first-year interns, $5.00 per year); Canada, $9.00 per year (Boston funds); foreign, $10.50 per year.

Microfilm volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

Material, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

FEDERAL DEPARTMENT OF HEALTH

Elsewhere in this issue of the *Journal* will be found an analysis of the relations of the physician to Federal medical services, as they are and as they will be, if the report of the Hoover Commission continues to be neglected. The paper is all the more important for having been delivered before the New England Postgraduate Assembly in Boston last fall, by Dr. Robert Collier Page, Chairman of the National Doctors Committee for Improved Federal Medical Services.

In 1949 the bipartisan Hoover Commission on Economy in the Federal Government delivered its exhaustive report to Congress. The Commission, composed of 17 members, had scrutinized the wasteful expenditure of $2,000,000,000 that the Federal Government had been appropriating annually for medical services through four large (Army, Navy, Veterans and Public Health Service) and thirty smaller systems caring for 24,000,000 persons. By way of remedying this chaotic state of affairs the commission had recommended a single Department of Health having central control and authority in the management, purchase, supply and construction of all existing health agencies of the Government. The improvements that this proposed reorganization might accomplish were envisaged as follows*:

> The general standard of federal medical care would be improved.
>
> There would be central supervision of major federal care, public health, and medical research activities. Unified responsibility is the key to good management. The President, the Congress, and the public could look to one man for the results.
>
> Construction costs could be standardized and reduced. Federal hospitals could be utilized to the fullest extent by eliminating present distinctions as to the particular types of beneficiaries for which each can care. After all, a patient is a patient, whether he is a veteran, merchant seaman, or in the Army, Navy, or Air Force.
>
> The medical manpower at the call of the federal government could be used to the fullest extent, and present deficits in skilled personnel could be greatly reduced.
>
> The need for any draft of medical manpower in time of peace would be greatly lessened.
>
> The cost of health and medical services would be clearly identified and known to Congress.
>
> The facilities of private hospitals and the skills of physicians in private life and in the universities could be utilized far more effectively than they are now.

What has happened to the Hoover Report and its courageous recommendations?

Currently coming up for hearings in Congress are Bills S. 1140 and HR. 3688 and 3305, which, if passed, would create such a department of health, headed by a Secretary of Health of cabinet rank. These bills have been awaiting hearings since March 15, 1951. Meanwhile, the Magnuson Commission has been appointed to survey the health needs of the nation. Since, in view of the stupendous nature of its task, a report from the Commission cannot be expected for many months to come, its appointment will have the effect of still further delaying action on the bills.

*The Commission on Organization of the Executive Branch of the Government. Medical Activities. Herbert Hoover, Chairman. Washington, 1941. P. 15.

Some of the arguments for and against S. 1140 and its companion measures are worth summarizing:

Opposition to the bills has been voiced by veterans' organizations on the ground that anything that "interferes" with the present medical care of the veteran is undesirable. Obviously, particular pressure groups would have less influence on the new hospital system than they now have on veterans' hospitals. It is probable, however, that the veteran and others eligible through connection with the armed forces would receive even better care than is now the case. Certain medical organizations oppose parts of the bill, some because they do not wish to face the veterans' opposition and others because the bill provides that the Secretary of Health be a layman. It is difficult to subscribe to the Commission's rosy view that "the President, the Congress and the public could look to one man for the results," especially if he were a layman. Many physicians consider it unnecessarily radical to include in the Department, as the bills provide, most of the military hospitals in the country.

The general advantages of the bills, however, which follow faithfully the recommendations of the Hoover Commission, are great. It is estimated that at least $150,000,000 could be saved annually. In addition, substantial benefits would accrue to physicians now working in Federal medical systems, career men, consultants and residents in training. Amalgamation of such specialized patient populations as now exist separately in veterans, military and public-health hospitals would provide to the physicians broader experience with patients more representative of the general population as regards age, sex and kinds of disease than is now the case in any one of these institutions.

It is reasonable to believe that the interests of the public, of those eligible for governmental care and of the physician will be promoted if the controversial aspects of the various bills scheduled for hearings can be harmonized with their courageous objectives. Certainly, the fruits of the Hoover Commission's industry should not be allowed to spoil on the vine.

NATIONAL TUBERCULOSIS ASSOCIATION

IT WILL be no ordinary meeting when the National Tuberculosis Association convenes in Boston during the last week in May, with Dr. Alton Pope in the chair. What was already scheduled as a full, active program will be fuller and more active after an unanticipated intrusion of the isonicotinic-acid derivatives into some of the sessions. Those sessions are supposed to be shorter this year than in former years, but they may be hotter, for the National Tuberculosis Association and its component groups have the most at stake among professional persons in attempting to evaluate these promising drugs in an all-too-brief testing period. Apparently, however, it is not too soon for the public to expect miracles and for talk to have started already about lopping some $313,000 off the Public Health Service budget for tuberculosis control.

For the most part the program is conventional, covering epidemiologic, clinical, specialized and nursing facets of the problem. Nontuberculous chest diseases — constrictive pericarditis, mitral stenosis and spontaneous pneumothorax — and bacteriologic and endocrine (ACTH and cortisone) aspects of the disease will be reviewed; one panel discussion will center on the intriguing subject "The Hospital Looks at Itself Through the Patients' Eyes."

Interesting as are the possibilities for the tuberculosis experts of 1952 to review what the past year has brought, the high point of the meeting will come when they convene to contemplate what changes are in store for the future. A special session presided over by Dr. Esmond R. Long, director of medical research of the Association, is scheduled for Monday evening, May 26, between 8:30 and 10:30 p.m. At that time a symposium has been arranged, at which Drs. Walsh McDermott, editor of the *American Review of Tuberculosis*, William Steenken of the Trudeau Laboratory and John C. Burke of the Squibb Institute for Medical Research will describe the development and study of the nicotinic-acid derivatives for tuberculosis. Clinical studies will be reviewed by staff members of the Sea View Hospital, New York Hospital–Cornell Medical Center and the Veterans Administration. Finally, the implications to health agencies and tuberculosis associations will be discussed by Drs. Robert J. Anderson and James E. Perkins.

NEW DRUGS FOR TUBERCULOSIS

In the past few years a number of relatively simple chemical substances, among them certain sulfones, some thiosemicarbazones and para-aminosalicylic acid (PAS), have been shown to be active bacteriostatic agents against tubercle bacilli *in vitro* and have also produced beneficial therapeutic effects in experimental tuberculous infections of animals as well as in human tuberculosis. Of the various chemicals mentioned, however, only PAS has gained any wide clinical acceptance in this country — and even this drug, because of its relatively low activity, has been recommended primarily as an adjuvant to streptomycin or for the treatment of streptomycin-resistant cases. Nevertheless, the activity of these various agents has raised great hopes that other simple, more highly active and nontoxic anti-tuberculosis drugs would soon be discovered, and many research laboratories set out to find such chemicals. Some of these hopes appear to have been realized, at least to some extent, in the group of nicotinic-acid derivatives, the most active of which appears to be isonicotinic-acid hydrazide (INH).

The discovery of this and related groups of active chemicals is the product of extensive screening programs conducted in the research laboratories of several large pharmaceutical manufacturers. As a result of such a program, it was reported in 1948 that nicotinamide, given as 0.5–0.75 per cent of the diet, will markedly suppress the spread of tuberculosis in experimentally infected mice. This activity was roughly equivalent to that produced by 1 mg. of streptomycin given four times daily over the same test period. Alterations in the chemical structure of this well known vitamin markedly reduced its anti-tuberculosis activity. Furthermore, there was evidence of the development of resistance to the nicotinamide after more than 5 mouse passages; there were indications, however, that streptomycin plus nicotinamide was more effective than either given alone.[1]

A continuation of these studies led to the investigation of derivatives of the closely related pyrazine; of the substances synthesized, pyrazinamide appeared to be the most active. Some reports on the effectiveness of this compound in tuberculous infections of mice and human beings were presented at the Eleventh Conference on the Chemotherapy of Tuberculosis in St. Louis last January and are to be found in the May issue of the *American Review of Tuberculosis*. In mice, pyrazinamide was found to have a therapeutic index of 500 and to be 7 times as active by weight as nicotinamide and several times as active as PAS. In guinea pigs it is about one third to one fifth as active as streptomycin, 4 to 10 times as active as PAS and 3 to 7 times as active as nicotinamide. Nearly all the chemical variations of pyrazinamide that were tested were found to be inactive.

In patients with active pulmonary tuberculosis, pyrazinamide produced rapid defervescence, followed by a lessening of the cough and of the total amount of sputum raised. It appeared to be equally effective in patients whose bacilli were sensitive or resistant to streptomycin. Extrapulmonary lesions showed a variable response; some, however, improved or healed rapidly and dramatically. Toxic reactions were mild and unimportant when a proper dosage regimen was used. Although tubercle bacilli were either reduced or eliminated from the sputum in more than half of the patients studied, at least during the brief period of observation, the usefulness of pyrazinamide appeared to be limited by the rapid emergence of markedly resistant bacilli in the far-advanced cases with large cavities.

Even more encouraging are the early results obtained with isonicotinic-acid derivatives, the most active of which appears to be the hydrazine (INH). Although the first reports of its clinical use unfortunately were prematurely released in the public press and over the radio, some of the preliminary laboratory and clinical findings concerning this compound have since been published. These papers form the complete issues of the *Quarterly Bulletin of Sea View Hospital* for January and *Diseases of the Chest* for April and comprise the major part of the April issue of the *American Review of Tuberculosis*. An editorial summarizing and commenting on the findings presented in these papers appears in the *Journal of the American Medical Association* for March 22; many of the authors of these articles and a number of other physicians have presented these and additional findings at many medical

meetings during this spring. A detailed and critical discussion of the subject is expected to take place at the forthcoming Boston meeting of the National Tuberculosis Association.

A concise summary of the preliminary data is contained in a statement prepared under the date of March 5, 1952, by the American Trudeau Society (Medical Section of the National Tuberculosis Association). Isonicotinic-acid hydrazide has been found to be markedly inhibitory to the growth of tubercle bacilli *in vitro* in concentrations that are much lower than those readily maintained during treatment. It is ineffective, however, against any other types of common pathogenic bacteria or protozoa. In experimental tuberculosis of mice, guinea pigs, rabbits and monkeys, it appears to be about as active as streptomycin. The toxicity of INH appears to be relatively low when given in the therapeutic range of dosage. The drug appears to be mostly excreted in the urine, and it reaches the serum, pleural fluid and cerebrospinal fluid rapidly.

Already there is evidence of the development of significant degrees of resistance both *in vitro* and *in vivo*, although some early reports suggested that the rate of emergence of resistance may be much slower than with streptomycin. Some observations already noted,[2] however, indicate that this may not be the case but that, on the contrary, significantly high degrees of resistance may develop rapidly and may be associated with relapse of activity of tuberculosis infections. Particularly revealing are some studies carried out with *Mycobacterium ranae*.[3] This organism was found to develop "complete" resistance to INH in a single step, just as it does to streptomycin; in fact, the incidence of INH-resistant mutants was considerably higher. Preliminary observations indicated that the mutation rate to INH resistance was more than 1000 times higher than in analogous experiments with streptomycin. However, combinations of INH with other anti-tuberculosis drugs or antibiotics produced an additive effect, and the emergence of resistance to each member of any combination was markedly delayed. Eventually, however, resistance to both agents did develop. There was no significant cross-resistance between INH and any of 24 other antibacterial agents, including all those known to have antituberculosis effects. Many more data on these aspects, however, are urgently needed, particularly in tuberculous patients under treatment.

In treated patients, the chief toxic effects of therapeutic doses are constipation and a number of neurologic and vasomotor manifestations, including hyperreflexia, difficulty in starting the urinary stream (in males), postural hypotension and dizziness. There is eosinophilia in some cases, an occasional reduction in circulating hemoglobin and the appearance of traces of albumin, a few casts and some reducing substance in the urine. Rashes have been infrequent, and there is no clear evidence of eighth-nerve damage or of any significant or lasting changes in renal or hepatic function.

The activity of INH in human tuberculosis is manifested in several ways. There is a reduction of fever to normal or nearly normal levels within two to three weeks in the majority of cases. The severity of the cough, the volume of sputum raised and the number of demonstrable tubercle bacilli are reduced. Appetite, strength and weight increase markedly. Clearing of pulmonary lesions by x-ray occurs in some cases, and there is an initial favorable improvement in nonpulmonary lesions, including fistulas, sinuses and mucous-membrane lesions, as well as in miliary and meningeal tuberculosis. Generally speaking, all these early results are comparable with early effects initially obtained with adequate doses of streptomycin.

The statement of the American Trudeau Society calls attention to the fact that there are many unanswered problems; their solution must await the accumulation of a considerably greater body of controlled data than are now available. This is particularly true with respect to long-term results, which must be evaluated in order to ascertain the place of these new agents in relation to the other drugs and antibiotics currently in use, and especially with respect to the accepted methods of rest and surgical management. In the present state of our knowledge, the demonstrated action of these new drugs, although highly encouraging, should not alter the basic principles of the treatment of tuberculosis as presently understood.

Meanwhile, the uncontrolled use of these seemingly effective agents, particularly in ambulatory patients who have chronic, fibrotic, cavitary lesions and are constantly extruding large numbers of tubercle bacilli is much to be deprecated and can be highly dangerous. The development of resistant tubercle bacilli in these patients may deprive them of the possible benefits of these very same agents if they were properly and efficiently used. Moreover, such usage may be most dangerous to persons who are exposed to such patients and who may become infected with these resistant bacilli. The danger is compounded, of course, in patients who already have received streptomycin or PAS or both and whose organisms have already become resistant to these latter agents. On the other hand, the lack of cross resistance with other anti-tuberculosis agents and the suppression of the development of resistance when INH is used in combination with such agents suggests a possible use of multiple chemotherapy that may prove even more effective than the combination of streptomycin and PAS.

References

1. McKenzie, D., Malone, L., Kushner, S., Oleson, J. J., and Subbarow, Y. Effect of nicotinic acid amide on experimental tuberculosis of white mice. *J. Lab. & Clin. Med.* 33:1249-1253, 1948.
2. Steenken, W., Jr., Meade, G. M., Wolinsky, E., and Coates, E. O., Jr. Drug resistant tubercle bacilli from patients treated with isonicotinic acid hydrazides. *J. A. M. A.* 149:187, 1952.
3. Szybalski, W., and Bryson, V. Resistance studies with derivatives of isonicotinic acid. *Microbial Genetics Bull.* No. 6:21, 1952. *Am. Rev. Tuberc.* (in press).

ATOMIC ACCIDENTS

A GRATIFYING and striking feature of the development of atomic energy has been the fine record of personnel health and safety achieved in this new, vitally important and potentially hazardous field. In spite of the temptation to cut corners and take chances, the policy of the Manhattan Engineer District in the past and now of the Atomic Energy Commission is continuing emphasis on protection of workers in the plants and of the adjacent general populations.

Elsewhere in this issue are reported the detailed clinical records of the only two fatalities and of the less severe injuries that have occurred from atomic explosions in the laboratories and plants.

Physicians can gain from this clear recounting of signs, symptoms and responses to therapy an understanding of the types of problems caused by ionizing radiation that might well be encountered in the survivors of an atomic explosion, either accidental or designed.

The entity of the acute radiation syndrome, uncomplicated by the blast injuries and flash burns that were present in many of the cases studied by the Joint Commission in Hiroshima and Nagasaki, is clearly presented.

A fully developed foetus was taken from the body of a woman at Utica, New York, who recently died at the age of 77. She had carried it 46 years! The particulars are promised.

Boston M. & S. J., *May 19, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BURNS — Thomas F. Burns, M.D., of Fall River, died on April 23. He was in his sixty-first year.

Dr. Burns received his degree from Jefferson Medical College of Philadelphia in 1912. He was a member of the Fall River Medical Association and a fellow of the American Medical Association.

He is survived by his widow and a son.

FLYNN — William A. Flynn, M.D., of Amesbury, died on April 12. He was in his fifty-fifth year.

Dr. Flynn received his degree from Tufts College Medical School in 1923.

He is survived by his widow and three children.

HOLBROOK — Charles A. Holbrook, M.D., of Haverhill, died on April 9. He was in his seventy-fourth year.

Dr. Holbrook received his degree from Harvard Medical School in 1908. He was a fellow of the American Medical Association.

He is survived by his widow and two children.

PITCHER — Hervey B. Pitcher, M.D., of Fitchburg, died on November 15, 1951. He was in his seventieth year.

Dr. Pitcher received his degree from Boston University School of Medicine in 1908.

He is survived by his widow.

CORRESPONDENCE

ARCHEOLOGIC TRIUMPH

To the Editor: Congratulations for your editorial of October 18, 1951, "Straw Man, Straw World."

It is good to know that some persons appreciate the seriousness of this terrible problem. I hope, however, that

STATE COLLEGE LIBRARY MAR 27 1952 MANHATTAN KANSAS APPLIED SCIENCE

you are not naïve enough to think that anything is going to be done about it.

It grieves me that when the archeologists of 500 years from now (if there is anybody left to be an archeologist) delve into the ruins of Boston they will find the *New England Journal of Medicine* perpetuating that slander about the burning of witches in Salem. It is my understanding that no one was ever burned in Massachusetts. The Salem "witches" were hanged.

A. L. SPRINGER, M.D.

San Juan, P. R.

Note: It is difficult to be naïve, those days, even about the history of Salem's Gallows Hill. Nineteen "witches," including a clergyman, were hanged and one was pressed to death, according to the records. None were burned in Salem. We will have to take our chances on anyone's finding a copy of the *Journal* in the ruins of Boston, 500 years hence. — ED.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Doctor's Pilgrimage. By Edmund A. Brasset, M.D. 8°, cloth, 256 pp. Philadelphia: J. B. Lippincott Company, 1951. $3.50.

Dr. Brasset tells the story of his work as a pioneer physician in a small town in Nova Scotia and of how he finally achieved his ambition to become a brain surgeon. The story is interestingly told, and the book should be in all collections of biography.

Revista Médica da Aeronáutica: Número especial consagrado à primeira Jornada do Serviço de Saude da Aeronáutica e comemorativo do primero decenio da criacao do Ministerio da Aeronáutica. Año III, Números 1 a 4. 8°, paper, 775 pp., with illustrations. Rio de Janeiro, Brasil: Diretoria de Saude da Aeronáutica, 1951.

Attention is called to this periodical on medical aeronautics, now in its third year. This part of Volume III contains a large number of articles on the various aspects of the subject.

NOTICES

REFRESHER COURSE FOR GENERAL PRACTITIONERS

The Dr. Nathan Sidel Teaching Fund has been established at the Beth Israel Hospital to offer tuition scholarship and a grant of $250 to general practitioners accepted for one month of clinical medicine during June, July, August or September. Further information may be obtained by writing to: Tufts Postgraduate Courses, Beth Israel Hospital, Boston.

MASSACHUSETTS SCHOOL PHYSICIANS' ASSOCIATION

The annual meeting of the Massachusetts School Physicians' Association will be held Thursday afternoon, May 22, in Parlor C of the Hotel Statler, Boston.

MASSACHUSETTS ASSOCIATION OF MEDICAL TECHNOLOGISTS, INC.

The Massachusetts Association of Medical Technologists, Inc., will hold its fourth annual meeting, under the auspices of the Greater Boston Medical Technologists Association, at the Hotel Somerset, Boston, on Saturday, May 24.

TUBERCULOSIS SYMPOSIUM

A tuberculosis symposium for general practitioners will be held at Saranac Lake, New York, July 14–18. This symposium, sponsored by the Saranac Lake Medical Society, will cover all aspects of the modern treatment of pulmonary tuberculosis. Meetings will be held during the mornings only; there will be elective activities during the afternoon. The only charge will be a $15.00 registration fee.

Further information may be obtained from the Saranac Lake Medical Society, Box 707, Saranac Lake, New York.

INTERNATIONAL ACADEMY OF PROCTOLOGY

The International Academy of Proctology will hold its fourth annual meeting in Chicago, June 6-8 at the Edgewater Beach Hotel.

SOCIETY MEETINGS AND CONFERENCES

MAY 11–17. Pan-American Convention of Gastroenterology. Page 434, issue of March 13.

MAY 16. New England Pediatric Society. Page 676, issue of April 24.

MAY 17–31. Springfield Hospital. Page 635, issue of April 17.

MAY 19–22. Massachusetts Medical Society. Hotel Statler, Boston.

MAY 19–23. Courses in Laboratory Diagnosis of Tuberculosis. Page 354, issue of February 28.

MAY 20. Children's Cancer Research Foundation. Page 676, issue of April 24.

MAY 20. Washingtonian Hospital Institute on Alcoholism. Page 760, issue of May 8.

MAY 21 AND 22. Venereal-Disease Seminar. Page 559, issue of April 3.

MAY 22. Massachusetts School Physicians' Association. Notice above.

MAY 22–24. American Academy of Pediatrics. Page 522, issue of March 27.

MAY 23. The New England Rheumatism Society. Page 760, issue of May 8.

MAY 23. The New England Veterans Administration Surgical Society. Page 760, issue of May 8.

MAY 24. Annual Meeting. Massachusetts Association of Medical Technologists, Inc. Notice above.

MAY 26–28. Minnesota State Medical Association. Annual Meeting. Page 316, issue of February 21.

MAY 26–29. National Tuberculosis Association. Sheraton-Plaza and Statler hotels, Boston.

MAY 29–31. American Academy of Dental Medicine. Page 476, issue of March 20.

JUNE 5. Boston City Hospital House Officers' Association. Page 760, issue of May 8.

JUNE 5. New York Society for Circulatory Diseases. Page 676, issue of April 24.

JUNE 5–8. American College of Chest Physicians. Page 280, issue of February 14.

JUNE 6 AND 7. American College of Cardiology. Page 760, issue of May 8.

JUNE 6–8. International Academy of Proctology. Notice above.

JUNE 7 AND 8. Society for Investigative Dermatology, Inc. Page 676, issue of April 24.

JUNE 18–20. Massachusetts Public Health Conference. Amherst.

JUNE 18–20. New England Health Institute. Page 760, issue of May 8.

JUNE 19–21. American Association of Genito-Urinary Surgeons. Page 434, issue of March 13.

JUNE 22–26. American Society of Medical Technologists. Twentieth Annual Convention. Portland, Oregon.

JUNE 23–25. Military-Civilian Medical Symposium. Murphy Army Hospital, Waltham.

JULY. Commonwealth and Empire Health and Tuberculosis Conference. Page 792, issue of November 15.

JULY 7–11. International Congress of Dietetics. Page 434, issue of March 13.

JULY 7–12. International Diabetes Federation. Page 316, issue of February 21.

JULY 8–11. Thirteenth British Congress of Obstetrics and Gynecology. Page 916, issue of December 6.

JULY 14–18. Tuberculosis Symposium. Notice above.

JULY 14–19. International Congress of Physical Medicine. Page 998, issue of June 28.

JULY 24–26. Conference on Aging. Page 559, issue of April 3.

AUGUST 25–29. American Congress of Physical Medicine. Page 476, issue of March 20.

AUGUST 31–SEPTEMBER 6. Interamerican Congress of Cardiology. Page 422, issue of March 27.

SEPTEMBER 7–9. Combined session of the New Hampshire and Vermont State Medical Societies. Mount Washington Hotel, Bretton Woods, New Hampshire.

OCTOBER 28–30. New England Postgraduate Assembly. Hotel Statler, Boston.

(Notices concluded on page xv)

1952

ciety,
onary
only;
The

ranac
k.

GY
ld its
water

ge 434,
pril 24.
Boston.
Page
ssue of
ge 760,
April 3.
above.
ssue of
, issue
Society.
Medical
Meeting.
za and
6, issue
ge 760,
issue of
ssue of
ssue of
ve.
ge 676,
erst.
May 8.
Page
entieth
Army
Confer-
ssue of
ssue of
cology.
ge 998,
ge 476,
Page
ermont
a, New
Statler,